The New England
Journal of Medicine

VOLUME 209 DECEMBER 21, 1933 NUMBER 25

NEW ENGLAND SURGICAL SOCIETY

APPENDICES EPIPLOICAE*

And Their Surgical Significance With Report of Three Cases

BY DANIEL C. PATTERSON, M.D.†

THE Appendices Epiploicae as a cause of surgical diseases have not received the attention they warrant. They are seldom mentioned in any of the textbooks. In a fairly recent work on the large intestines they are dismissed with the statement, "they are of no surgical significance". Drs. Rankin, Bargin and Buie[1], however, in their recent book, devote a chapter to their consideration. Most of the articles and reports of cases have come from European authors.

The pathological history of these little tabs of fat is rather interesting. According to all previous papers, Littré[2], in 1703, found a small white stone the size of a pea free in the abdominal cavity of a cadaver he was dissecting. No evidence was presented to show that this was an appendix epiploica, but it appears to be accepted as the first case report.

Deville[2], in 1851, exhibited before the Anatomical Society five foreign bodies found free in the peritoneal cavity, and mentioned casually that the transverse colon contained an appendix epiploica that was on the verge of becoming detached, and that it bore a striking similarity in appearance to the foreign bodies. He did not, however, associate the two conditions.

Virchow[2], in 1863, was the first to demonstrate the pathological relationship between the foreign bodies and the appendices epiploicae. He claimed that as a result of obesity or an infection, an increased amount of fat is deposited in the appendices epiploicae; that the fat undergoes calcification which causes an increase in weight. This in turn leads to obstruction of the blood vessels of the pedicle, necrosis occurs, and the freed appendices epiploicae fall into the peritoneal cavity.

In 1894 Cruveilhier[2] reported a case of a foreign body of extreme hardness, white and smooth, the size of a billiard ball, found in the abdomen of a soldier dead of an unknown illness. Again there is nothing to prove that this was a calcified appendix epiploica. Its large size would suggest some other origin.

In 1905 Reidel[2] reported several cases. In one an appendix epiploica with a twisted pedicle was found in a hernial sac. In another an inflamed, adherent appendix epiploica had caused intestinal obstruction. These appear to be the first cases reported of disease, other than the finding of loose bodies.

In this country, W. A. Briggs[3] reported a case in 1908 of a gangrenous appendix epiploica which caused symptoms simulating an appendicitis, and was cured by operation. In 1915 A. R. Kimpton[4] reported a similar case.

In 1917 A. H. Harrigan[5] of New York reviewed the literature and reported a case of an inflamed appendix epiploica with a twisted pedicle that had caused an acute abdominal crisis, requiring operation. He gives very interesting abstracts of previously reported cases, and I have made free use of his historical data.

In 1919 V. C. Hunt[6] also reviewed the literature and found forty-two (42) reported cases of diseases of these organs. He added eleven (11) cases from the Mayo Clinic seen in ten years. In most of these cases the diseased appendix was an incidental finding at operation for some other condition.

In 1924 P. Klingenstein[7] reviewed the history of diseases of the appendices epiploicae and reported four (4) cases from Mt. Sinai Hospital in New York. In two (2) of the cases the appendix epiploica was incarcerated in a hernial sac. In one (1) a twisted appendix was found adherent to a perforated appendix vermiformis. In the fourth case a twisted and acutely inflamed epiploic appendage was discovered at autopsy in a case of acute hemorrhagic pancreatitis. He found recorded at that time twelve (12) cases of foreign bodies; seventeen (17) cases of intra-abdominal torsion; ten (10) cases of intrahernial torsion; thirteen (13) cases of intrahernial incarceration; and three (3) cases of intestinal obstruction due to adherent appendices epiploicae. Since his publication there have been reported fifteen (15) cases of torsion of appendices epiploicae; four (4) cases of intrahernial strangulation; and two (2) cases of intestinal obstruction. I feel sure there have been quite a goodly number of unreported cases as I can add one to each of these groups.

The appendices epiploicae are small pouches of peritoneum filled with fat. Bland Sutton describes them as "localized, pedunculated overgrowths of subserous fat directly continuous with the fat in the mesentery." They are found along the mesentery of the appendix and on

*Read at the meeting of the New England Surgical Society at Boston, September 30, 1933.

†Patterson — Attending Surgeon, Bridgeport Hospital. For record and address of author see "This Week's Issue," page 1298.

the large intestine as far as the rectum. As a rule they are arranged in two rows along the anterior and the posterior inferior longitudinal bands, and are more numerous and larger on the sigmoid than elsewhere. They vary in size and shape. Some have been reported 15 cm. in length, but the average is 3 or 4 cm. They may be cylindrical, flattened or lobulated. According to Robinson[8], who made an extensive study of them in 1908, they are present at birth.

They have been credited by some writers with a protective function similar to the omentum. This conclusion was drawn because they have been found adherent to inflamed organs, but such a relationship is a natural consequence of infection. Robinson[8] pointed out that their structure is so unlike the omentum that it is improbable that they have the same function. After experimental studies he suggested that they might have some function in relation to the movement and absorption of fluid from the large intestine. The thought occurred to me that they might act simply as bumpers for the large intestine, fending this organ from the parietes and the other viscera, thus facilitating peristalsis. Their location and simple structure would support such a view.

Any infectious process in the abdominal cavity may affect the appendices epiploicae from contact, and they become involved in the inflammatory process, acting as a rule to wall off the seat of infection.

The diseases that may affect the appendices epiploicae primarily are the following:

(1) Inflammatory changes.
(2) Torsion of the pedicle.
(3) Calcification and formation of loose bodies.
(4) Incarceration in a hernial sac, with or without torsion.

I have seen no reports where malignant changes had occurred.

(1) INFLAMMATORY CHANGES

When the inflammatory process is primarily in the appendix epiploica, it is probably the result of interference with its blood supply from torsion of the pedicle, or it may be an invasion of micro-organisms from the colon. While there is no direct connection between them and the lumen of the bowel, they are undoubtedly infected at times from this source. They have been found inflamed in cases of diverticulitis. Erdmann[9] found one or more involved in most of his cases of acute diverticulitis. Greaves[10] reported a case of an inflammatory process in two appendices epiploicae of the pelvic colon. Each contained a fecal concretion, but no communication with the lumen of the bowel could be found. That isolated infection does take place in these organs is evident, as several cases have been reported where in a diagnosis of appendicitis the abdomen has been opened and the only finding has been an inflamed gangrenous appendix epiploica.

Colon bacilli have been obtained both from the twisted appendices and from the loose bodies. The inflamed appendices may go on to abscess formation, and may possibly be the cause of some of the unexplained cases of peritonitis. They may become attached to the parietes or adjacent viscera and cause intestinal obstruction. This occurred in one of my cases.

Mrs. H., a woman 84 years of age, and the mother of seventeen (17) children, was admitted to Bridgeport Hospital in March, 1925 giving a history of previous illness from chronic bronchial asthma. The present illness began five days before her admission. She was taken with sudden pain in the lower abdomen which was followed shortly by nausea, vomiting and obstipation. Examination showed her to be a fairly well developed and nourished old woman who was acutely ill. The abdomen was slightly distended. There was marked tenderness throughout. She was vomiting dark brown material and had passed no gas by rectum. A barium colon roentgenogram was made, but this was negative except for a single small diverticulum in the sigmoid. Complete obstruction was present. A laparotomy was done under local anesthesia. The small intestines were ballooned and a loop of the lower ileum, of dark reddish color, was found strangulated in the lower abdomen. An inflamed appendix epiploica was found with its distal end adherent to the pelvic brim, just to the right of the midline. The obstructed loop of bowel had passed beneath this band and was on the edge of viability. There was no other evidence of inflammation in the abdomen. The appendix epiploica was removed, the obstructed loop relieved, and the abdomen closed. The patient made an uneventful recovery. She was treated at the hospital over a year later for bronchitis, but had no further abdominal complaints.

(2) TORSION

The most frequently reported disease of the appendices epiploicae has been intra-abdominal torsion. According to Harrigan, Cruveilhier was the first to establish this condition as a definite entity. It has been the only pathological finding at laparotomy in some cases of acute abdomen, and cure was obtained with removal of the appendage. The symptoms in most instances simulated appendicitis. However, in most of the cases that have been reported, the twisted appendix epiploica has been found during the course of an operation for some other condition, and was apparently creating no disturbance.

Several theories have been advanced to explain why torsion takes place. Morestin[11] states that for torsion to occur it is necessary that the appendage should be abnormally long and large. I have a specimen which I removed recently that is less than an inch long. It was undoubtedly much larger before torsion occurred, for its pedicle was quite wide, and it is difficult to visualize how the twisting started.

Payr's[11] theory is that when stasis and engorgement take place, the vein, being longer

than the artery by reason of its tortuous course, furnishes a tendency for the twisting of the pedicle. Other causes, such as peristalsis, variations in the filling of the abdominal organs, and the effect of pressure, have been mentioned. Hunt suggested that infection might be the etiological factor in torsion.

Seven (7) of the cases reported by Hunt were true torsions of the appendices epiploicae; four (4) of these cases presented acute symptoms for which operation was done; and three (3) were found during operations for other conditions, and were probably symptomless. This was the condition found in my case. Torsion of an appendix epiploica may be sudden or gradual. If sudden, it will give rise to acute symptoms suggestive of appendicitis, diverticulitis, or tubo-ovarian disease. If gradual, it should cause no disturbance.

Mrs. B., a housewife, 44 years of age, had no complaints except for a menorrhagia of one year's duration. She was a large woman, weighing 190 pounds, and the examination was negative except for a fibroid on the anterior surface of the uterus. Hysterectomy was performed. Before closing the abdomen, I noted the abundance and large size of the appendices epiploicae. On the upper part of the sigmoid one of the appendages was found that was shrunken and hard. The pedicle, which was quite wide—though thin—had undergone a three-quarter turn, about half an inch from its attachment to the bowel, and had evidently cut off the blood supply. This appendage would probably have become a loose body in the peritoneal cavity if left alone. I questioned the patient later, but she had never had any symptoms referable to her left colon. (The specimen is here if anyone would like to see it.)

(3) LOOSE BODIES

When the blood supply is shut off through torsion, there is a splitting up of fat, and calcification takes place, the pedicle atrophies, and the appendage drops from its attachment to the colon and becomes a loose body. This may not be the only source of loose bodies in the peritoneal cavity, but the evidence of Virchow and others demonstrates that such bodies do originate from the appendices epiploicae. These loose bodies vary greatly in size. Most of those reported were small, but some have been found as large as a hen's egg.

Some still show the presence of fat while others are fibro-cartilaginous and some calcified. Cruveilhier pointed out the similarity between them and the loose bodies of the joints. Laverean at autopsy found a mass of twelve (12) cartilaginous bodies in one case.

These bodies probably cause little or no disturbance unless infected, but that they do become infected is illustrated by one of Reidel's cases. The patient, a female 41 years of age, showed a severe peritonitis at operation. An appendix epiploica attached to the descending colon, with a flat, gray foreign body lying free between it and the abdominal wall, seemed to be the only cause of peritonitis. Colon bacilli were obtained from the foreign body, which was composed of fat. The patient died, and autopsy revealed no other cause of the peritonitis.

(4) IN HERNIAL SACS

Klingenstein states that Malgaigne and Cruveilhier were among the first to point out the possibility of the appendices epiploicae being the sole content of a hernial sac. The appendages have been found in femoral and umbilical hernias as well as inguinal, though the condition would naturally occur most frequently on the left side. They might remain in the hernial sac for a long time without causing trouble, or until torsion or strangulation occurred, when acute symptoms necessitating operation would arise.

R. E. Smith[12] in 1923 reported two cases where the appendix epiploica was attached to the fundus of a hernial sac, pulling part of the pelvic colon into the sac, and causing partial strangulation; also, giving rise to hemorrhage from the bowels. The following case occurred on my service at the Bridgeport Hospital.

Mrs. C., employed in a local factory, gave a history of previous good health. On July 17, 1933, about 4:00 P.M. she was lifting a box weighing 30 pounds when she felt severe pain in the left groin: as she put it "as if someone shot me." She reported at once to the dispensary, but aside from tenderness nothing was found by the examining physician. She had considerable pain during the night. She had no nausea or vomiting and had a normal bowel movement. On the eighteenth, pain was still present and a diagnosis of hernia was made by her physician. I saw her that afternoon. She was a rather obese woman, with a thick abdominal wall. There was marked tenderness over the left inguinal region, and a tumor about an inch in diameter was present at the inguinal ring. This was exquisitely tender and irreducible. There was no impulse on coughing. My impression was that the hernial sac contained incarcerated omentum. At operation, when the fascia was incised at the neck of the sac, the contents of the sac slipped back into the abdominal cavity. The neck of the sac easily admitted my finger. Exploration of the abdominal cavity with the finger revealed a firm mass which filled the pelvis. The abdomen was opened through a Pfannenstiel incision. As I use a transverse incision for inguinal herniae this was easily done. Just beneath the hernial opening was an appendix epiploica about 3 x 5 cm. in size. It was hemorrhagic and the pedicle showed evidence of traction. It was not twisted, however. It was removed, and microscopic examination showed marked engorgement of the blood vessels with considerable interstitial hemorrhage.

The pelvic mass proved very interesting. The left tube was the seat of a hematosalpinx that was twisted five complete turns. On the right side there was a hydrosalpinx five inches long and over an inch in diameter. These were removed and the abdomen closed. The patient made an uneventful recovery, leaving the hospital on the twelfth postoperative day.

DIAGNOSIS

The diagnosis of any of these diseases of the appendices epiploicae is quite impossible except at operation. Even then its presence might be

overlooked. The symptoms may simulate most any abdominal disease, especially diverticulitis. In some cases where the diseased appendage was on the sigmoid the symptoms and signs pointed to appendicitis. Where the appendage is in the hernial sac and torsion or strangulation has taken place, it cannot be distinguished from any other type of irreducible hernia.

I believe that disease of the appendices epiploicae is more frequent than we realize, and the possibility of its presence should always be borne in mind. They are probably responsible for some of the abdominal disturbances that recover without a diagnosis or operation. Where the degeneration is a slow process, as it no doubt was in my case of torsion, there are no symptoms, and unless another condition necessitates an operation, they would go undiscovered. These are merely surgical incidents, and, causing no symptoms, can hardly be classed as a disease. When conditions warrant, the appendices epiploicae should be inspected during laparotomy and if they show evidence of degeneration they should be removed. They should also be considered when exploration of the abdomen fails to reveal any of the usual seats of disease responsible for acute abdominal symptoms.

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DISCUSSION

DR. DAVID CHEEVER, Boston, Mass.: Somebody paid me quite a compliment when he asked me to discuss this paper, inferring that my experience was so large that I must have seen something of the rare condition, but, as is usually the case when a very careful paper by a man like Dr. Patterson has been written, practically all my information about the subject comes from his communication and in the two days which I had at my disposal, I haven't been able to find in the records of the Brigham Hospital anything about primary disease of the appendices epiploicae.

It is interesting to speculate on the function of any organ. There is, I think, the idea that the appendices have something to do with the absorption of water and fluid from the large intestine. That seems to me hardly plausible. It occurs to me to remind you that the large intestine differs from the small, by the presence of the haustra or pouches separated from each other by deep creases, and the appendices epiploicae sometimes seem to lie in the creases and thus interpose themselves between the different haustra. Whether this serves any useful function I do not know.

There is a little plausibility furnished to that by the fact that the appendices are uncommon on a cecum. They increase in number as you go along the colon where the haustra increase. These appendices have just one function, however, that I personally know about and that is they enable you to identify what part of the colon you are dealing with.

A good while ago I went down to Portsmouth, New Hampshire, and operated on a case of appendicitis in a family who summered there. One of our now deceased members in Portsmouth had been called to the case and made the diagnosis, and I should think might have felt chagrined at my being called, very much of a youngster, from Boston, on a case he was more capable of operating on than I.

I made a small incision, couldn't find the appendix, started to withdraw the cecum, and withdrew a good deal of very mobile cecum, until I suddenly realized that it was the sigmoid—which I should have known from the numerous appendices epiploicae which were there—and as I put it back, the other physician said rather grimly, "I thought so."

Mr. President, there are a great many appendices epiploicae in every person. They are useless. If they will become the seat of primary disease and twist and become inflamed, all I can say is, thank Heaven for the appendices epiploicae and for Dr. Patterson.

DR. RALPH B. OBER, Springfield, Mass.: About ten days ago I thought I had found a new disease and Dr. Patterson has just outlined the whole thing. I should like to place on record the description of this case.

On September 21 Dr. Fred Hagler, of Springfield, asked me to see the following case: A woman, aged 45, well nourished and developed, society golfer, played in a tournament September 19th, and partook of a full meal that evening. On September 20th, at 6:00 A.M., she woke with pain in the lower abdomen on the left side below the umbilicus. There was some nausea but no vomiting. She remained in bed all day with heat applied to the abdomen. At 6:00 P.M. she had temperature 99°, pulse 72 and showed tenderness and rigidity in the left lower quadrant.

An enema produced fair results. Food was withheld and heat continued. Previous history was neg-

ative as to any similar attack. There had been no alteration in function of bowel or menses, which latter occurred two weeks before.

On September 21 there was considerable rigidity and tenderness in lower left abdomen. The patient seemed to be in pain but her condition seemed good, T. 98.6°, P. 90. No particular pelvic tenderness, but examination showed a knob on the anterior part of the uterus. On account of rigidity nothing could be made out in the adnexa. Abdomen was rather stout.

Through the day the local symptoms remained the same. At the hospital her blood and urine were essentially normal. The persistence of symptoms and the local signs led to the diagnosis of either twisted pedunculated tumor of the uterus or ovary, or diverticulitis.

Operation by Dr. Hagler at 4:00 P.M. on September 21 showed a thin, blood-stained fluid in the abdomen, pelvis normal except for a small uterine fibroid anteriorly. The sigmoid was somewhat distended and adherent in the left iliac fossa. When delivered it showed a black necrotic epiploic appendage the size of a quarter. No apparent reason was seen for this. It was easily removed and showed no connection with the lumen. Its area of contact with the peritoneum was slightly ecchymotic and congested. A kinked and somewhat adherent appendix was also removed.

The patient has shown a normal convalescence since.

I am passing the specimen of the necrotic appendage about for inspection. Neither Dr. Hagler nor I had seen a similar case though several are reported in the literature. At the time this report was written I had not heard Dr. Patterson's paper.

Dr. Walter C. Seelye, Worcester, Mass.: I should like briefly to refer to my one and only case of appendices epiploicae, a man of middle age, with three or four days of symptoms of abdominal pain, diagnosed as acute appendicitis, with peritonitis.

A median incision was made in this man. He was stout with a large abdomen, and the appendix was found normal or practically normal. Upon a little further exploration, the sigmoid flexure was found nearly over to the median line in an abscessed mass, some of the pus having spilled free into the abdomen, showing general peritonitis.

Exploration of this abscessed cavity, showed a perfectly definite one of these appendices epiploicae, with two or three others adjoining it, partly inflamed, and the one in the middle was gangrenous and evidently the cause of the abscess and of the peritonitis.

The cause of this appeared to be due to torsion of the appendage. This was removed with one on each side of it, and the man died a few days later of peritonitis.

It led me to realize that this is an actual pathological entity although a rare one, and I feel that it is worth while to bear it in mind when operating for peritonitis with an unknown cause.

Dr. Michael F. Fallon, Worcester, Mass.: I wish to bear testimony to the occurrence of inflammation in the appendices epiploicae.

I had such a case in a physician four or five years ago. He had abdominal symptoms located in the left lower quadrant and such symptoms as you would find in the right lower quadrant in acute appendicitis.

We found, on operation, a definitely gangrenous appendix epiploica on the sigmoid flexure and the surrounding serosa inflamed and the neighboring appendices epiploicae partly inflamed.

We took this gangrenous appendix epiploica out.

We ruled out the appendix at the time finding it was normal and absolutely nothing pathological about it, so while a gangrenous appendix epiploica is a definite entity, it is so rare that it would hardly be advisable for young surgeons to take it up as a specialty.

Dr. Lyman Allen, Burlington, Vt.: I want to ask whether it isn't frequent that there are small diverticula extending into the appendices epiploicae, and whether diverticulitis and inflammation of the appendices are not closely connected.

NEW ENGLAND HEART ASSOCIATION

THE PHYSIOLOGY OF THE PULMONARY CIRCULATION*

BY HERRMAN L. BLUMGART, M.D.†

WHEN a healthy individual passes from a condition of rest to active muscular effort, the blood flow through the lungs increases from five to twenty-five liters. This increased blood flow through the lungs is adequately oxygenated by increased respiration and the heart rate is accelerated. The changes that occur in the pulmonary circulation under such physiological conditions, and their relation to derangements in disease, will be the subject of our attention during the next few minutes.

Like all other fluids, blood flows from areas of greater pressure to areas of lower pressure. The pressure in the pulmonary artery is derived from the contraction of the right ventricle. The pulmonary arterial blood pressure is approximately one-fourth of that in the systemic aorta. The pulmonary artery and its branches follow the general course of the bronchi and finally subdivide into the vast capillary bed in the alveoli of the lungs. This capillary bed is beautifully adapted to the respiratory function it subserves; the surface area of this capillary network has been estimated to be 44,000 square inches. The minute vessels in the lung offer relatively little resistance to the forward flow of blood. The lungs are drained by the venous tributaries which lead to the four pulmonary veins which empty into the left auricle.

The blood supply of the lungs is somewhat peculiar in that there is a second system of blood supply, i.e., that of the bronchial arteries and veins. The bronchial arteries usually number three, but vary from two to four in number. They arise from the thoracic aorta and supply nutrition to the bronchi and their subdivisions. The bronchial arteries, as well as the bronchial veins which empty into the azygos system, communicate freely by anastomoses with the pulmonary arteries and veins.

The regulation of the blood supply through the lungs is mainly a passive one. Vasomotor

*Read before the New England Heart Association, Boston, April 5, 1933.

†Blumgart — Visiting Physician and Director of Research, Beth Israel Hospital. For record and address of author see "This Week's Issue," page 1298.

fibers have been observed by anatomists, but active contractions of the pulmonary blood vessels have never been conclusively demonstrated, although under certain conditions, such as anaphylactic shock, vasoconstriction is said to be present.

The blood flow through the lungs is influenced to an important degree by the output of the right ventricle, and also of course by the inflow of blood into the right auricle, for obviously the right ventricle cannot eject what it does not receive. In health, the adjustment between the output of the right and left ventricle is accomplished very nicely, for pulmonary engorgement does not occur, and so we may assume that the output of both ventricles is essentially equal. In conditions, however, where there is failure of the left chambers of the heart because of aortic insufficiency, arterial hypertension or mitral stenosis, more blood is evidently pumped into the pulmonary circulation by the right ventricle than leaves this circulation by way of the pulmonary veins. Acute or chronic engorgement ensues and may progress to the stage of actual pulmonary edema. With engorgement of the pulmonary circulation from such causes, or indeed from any other causes, the elasticity of the lungs is diminished because of their distention with blood under increased pressure, respiration is interfered with, and dyspnea becomes evident.

The forward flow of blood through the pulmonary circulation is also affected by the respiratory movements, blood flow being facilitated by inspiration and somewhat impeded by expiration. This is shown by the well-known rise in systemic arterial blood pressure during inspiration, and its fall during expiration. The diaphragm likewise facilitates the blood flow through the lungs because in its descent during inspiration intra-abdominal pressure is raised, the intra-thoracic pressure becomes lowered, and the entrance of blood into lungs from the periphery is thereby facilitated.

Measurements of the volume of blood flow through the lungs have been made in man by various investigators during the last few decades. The most important influence which leads to increased pulmonary blood flow is an increase in the general metabolic rate of the body. This close inter-relationship between metabolism and blood flow is clearly evident in patients suffering from thyrotoxicosis. In a series of such patients the basal metabolic rate averaged 33 per cent above the normal and the velocity of blood flow through the lungs was 83 per cent above the average of normal. The greatly increased work of the heart even under basal conditions serves to explain the frequency of circulatory insufficiency in such patients. With lowering of the metabolic rate by the administration of Lugol's solution or by thyroidectomy, the slowing of blood flow was in every instance proportional to the fall in metabolic rate. These findings afford a rational explanation for the conspicuous alleviation of the clinical signs and symptoms of circulatory insufficiency frequently observed following these therapeutic measures.

In patients with myxedema the metabolic rate is lowered below normal and, similarly, the velocity and volume of blood flow are greatly diminished. The blood flow, while lessened, is nevertheless adequate for the abnormally low needs of the tissues. The heart may be able to perform the relatively small amount of work required under such circumstances but may be incapable of meeting the increased demands when the metabolic rate is raised toward normal. Such patients may show none of the evidences of circulatory insufficiency while the metabolic rate is low but may develop alarming signs and symptoms of circulatory failure following the administration of thyroid extract. The necessity for cautious administration of thyroid substance and the frequent advisability of previous digitalization are apparent. These considerations also illustrate the importance of a reduced metabolism in patients with cardiovascular disease.

Similar considerations apply to other states in which the metabolic rate may be elevated. Digestion, emotion and exercise are attended by an increased metabolism and the occurrence of attacks of angina pectoris and other evidences of circulatory insufficiency under such circumstances are more readily understood and more intelligently treated on the basis of the studies of the velocity and minute volume blood flow through the lungs.

Certain other conditions impose an increased amount of work on the heart. Epinephrin, for instance, after its subcutaneous administration, produces an increased velocity of blood flow through the lungs and a rise in the metabolic rate. Such findings support the clinical caution exercised by many in prescribing epinephrin for patients with circulatory insufficiency.

Mention should also be made of the mechanical filtration effect of the lungs in preventing bacteria, emboli, etc., which arise in the veins or the right chambers of the heart, from reaching the larger circulation. The importance of this fact has been shown in physiological experiments by Drinker, and recently we have been interested in observing patients with subacute bacterial endocarditis with involvement of only the right chambers of the heart.

ROENTGEN STUDY OF THE PULMONARY CIRCULATION IN HEALTH AND DISEASE*

DR. Hugo Roesler† discussed the increasing importance of the x-ray study of the pulmonary circulation. He illustrated the points which he made with many lantern slides. Investigation of the cardiac patient by fluoroscopic study as well as by use of x-ray films was shown to reveal important changes in the hilus shadows and the pulmonary artery. The importance of pulmonary hypertension is becoming more evident, particularly in relation to left heart failure. Such studies are also valuable in congenital heart disease.

*Abstract of paper read at the meeting of the New England Heart Association at Boston, April 5, 1933.

†Roesler—Associate Professor of Medicine, Temple University Medical School, Philadelphia. For record and address of author see "This Week's Issue," page 1298.

PATHOLOGICAL AND CLINICAL ASPECTS OF THE PULMONARY CIRCULATION*

BY PAUL D. WHITE, M.D.,† AND OSCAR BRENNER, M.D.†

PULMONARY vascular pathology is common but disease or disability resulting from it is rare. On the other hand disorders of the pulmonary circulation are of frequent occurrence but they are almost invariably the result of extrinsic causes. It is our plan now briefly to take up first pathology of the pulmonary blood vessels and its clinical significance, then the clinically more important conditions of pulmonary embolism and thrombosis, and finally the common and often serious states of pulmonary hypertension and congestion resulting from heart disease.

Our remarks on pathology of the pulmonary blood vessels are based on work done by one of us (Brenner) while at the Massachusetts General Hospital from April to November, 1931‡. A monograph on the subject is now being completed. From a summary of the data we shall give herewith a few of the findings and conclusions.

Though many individual cases of pulmonary vascular disease are to be found reported in the literature, practically no systematic work on this subject, with adequate controls, appears to have been done. It was largely in the hope of providing a base line for subsequent investigations that the present work was undertaken. A hundred consecutive unselected autopsies were taken and the changes in the pulmonary vessels, both naked eye and microscopical, were carefully compared with the clinical symptoms as recorded in the case sheets, and with the other pathological findings, especially in the heart, lungs, and systemic vessels. Measurements were made on the autopsy table of the circumference of the stem of the pulmonary artery, of its right and left branches, of the pulmonary veins, and of the aorta. Microscopical measurements were made, with the aid of a micrometer eyepiece, of the thickness of the stem of the pulmonary artery and of each of its three coats. Similar measurements were made in the case of the aorta and main pulmonary veins, and at the same time the diameters and thickness of the walls and of the various layers of the walls of several of each of the large arteries, small arteries, "arterioles", small and large veins in each lung were measured. Any pathological changes present were noted in each case.

Of the 100 cases studied 59 were males and 41 females. All ages were represented: there were 5 cases in the first decade of life, 9 in the second, 5 in the third, 11 in the fourth, 13 in the fifth, 23 in the sixth, 20 in the seventh, 12 in the eighth, and 2 in the ninth. The series of 100 cases was analyzed as to the presence of heart disease, pulmonary disease, and systemic hypertension; 33 cases showed none of these conditions, 7 showed heart disease without hypertension, 9 hypertension, 3 both hypertension and heart disease of other etiology, 29 lung disease, 11 lung and heart disease, 5 lung disease and systemic hypertension, and 3 lung disease, heart disease, and systemic hypertension.

Naked eye changes in the pulmonary vessels were found in 68 of the 100 patients (41 males or 70 per cent, and 27 females or 66 per cent). The changes varied from a few small, flat whitish patches in the main intrapulmonary branches of the pulmonary artery, to many large projecting, yellowish patches so numerous as to be almost confluent, and extending from the stem to the smallest intrapulmonary branches that could be traced. The lesions were almost always most marked in the main intrapulmonary branches, and were often confined to these vessels, the stem and the right and left arteries usually being free from naked eye change. When changes did occur in the stem they were usually slight and were usually confined to two spots—one imme-

*Read before the New England Heart Association, Boston, April 5, 1933.

‡We gratefully acknowledge the coöperation and kindness of Dr. Tracy B. Mallory, Pathologist at the Massachusetts General Hospital, who made this study possible for us.

†White—Physician, Massachusetts General Hospital. Brenner—Physician, Queen's Hospital, Birmingham, England. For records and addresses of authors see "This Week's Issue," page 1298.

diately above the valve cusps, the other just proximal to the point of bifurcation. The most important factor apparently in the causation of the changes in these 68 cases was age, for the older cases of all the groups, those with heart or lung disease or both, as well as those without either heart or lung disease, were the ones more often to show naked eye changes in the pulmonary vessels. Thus, of all the patients under the age of 50, only thirty-seven per cent (16 out of 43) showed changes, while of those over that age ninety-one per cent (52 out of 57) were abnormal. Eighty per cent of the cases over 40 years of age without either heart or pulmonary disease showed naked eye changes in the pulmonary vessels. The frequency of these changes was not appreciably increased by the presence of heart disease, chronic pulmonary disease or systemic hypertension, although the severity of the changes appeared to be somewhat increased; the combination, however, of two or three of these abnormal factors did favor an increase in incidence as well as severity. It thus seems fairly clear that in the pulmonary circulation as in the systemic, old age alone may be a cause of arteriosclerosis.

Microscopic changes were found in the pulmonary vessels in the great majority of cases, including all but three of the entire 100; those three patients were under ten years old. The small muscular arteries were involved microscopically in all but seven of the thirty-two cases showing no naked eye changes in any pulmonary vessels and in 90 per cent of the entire series of 100. The microscopical pathological changes in the arteries have been classified as follows: (1) arteriosclerosis (a) secondary, (b) primary, (2) endarteritis obliterans, (3) splitting and multiplication of the elastica interna, (4) endothelial proliferation, (5) hypertrophy of the media, (6) fibrosis of the media, (7) syphilis of the pulmonary arteries, (8) tubercle of the pulmonary arteries, (9) rheumatism of the pulmonary arteries, (10) acute septic arteritis, and (11) new growth. Changes in the arterioles and venules, which vessels, 0.1 mm. in diameter and under, we were surprised to find are distinguishable in the lung only when seen joining an artery or a vein, included (1) sclerosis, (2) infections, acute and chronic, and (3), new growth; these same changes were also found in the larger veins.

The commonest microscopic lesion of all was *sclerosis,* which was frequently found without heart or lung disease. Such a lesion is usually not dignified by the name of primary pulmonary sclerosis as it should actually be but has become applied only to a very limited group with extensive obliterating lesions and marked hypertrophy and sometimes failure of the right ventricle. One case of the 100 analyzed here showed this extreme degree of primary sclerosis or endarteritis obliterans which is allied to the so-called "black cardiacs"; that was a boy aged 11 years, the cause of whose pulmonary vascular disease was a mystery even after careful study; there was no evidence of syphilis, nor was there any of rheumatism except that the lesions in the vessels themselves were compatible with the latter infection. Sclerosis of lesser degrees involves pulmonary vessels of all sizes from the stem of the pulmonary artery to the smallest arterioles and from the venules to the main pulmonary veins.

Macroscopic and also microscopic sclerosis in the stem of the pulmonary artery was little if at all increased in frequency and severity by the presence of systemic hypertension; it did tend to increase with age more than with any other factor in this series. Microscopic sclerosis in the small muscular arteries is almost constantly present after the age of 40; before that age its frequency and severity are increased by the presence of heart or lung disease or by both; it was found in 90 out of the 100 cases of the present series. The arterioles and venules showed some degree of sclerosis in an even larger number of the cases, actually 94 per cent; these vessels were affected more often than any others but changes in the small veins were almost as frequent, occurring in 90 out of 99 patients and practically constant after the age of 40, often reaching a severe grade. Microscopic sclerosis in the large veins was considerably less common, occurring in only about half of these consecutive unselected cases (actually in 52 per cent of 89 patients); it was found in only nine of 29 cases without heart or lung disease (in three out of 14 under the age of 40 and in six out of 15 over that age), but in 14 of 24 cases with lung disease, and in 11 of 13 cases with both lung and heart disease.

A second important phase of this pathological study consisted of macroscopical and microscopical examination of the systemic vessels, particularly the aorta, coronary, renal, and splenic vessels in all 100 cases. No correlation with the changes in the pulmonary vessels could be found apart from the fact that sclerosis increased with advancing age in both sets of vessels.

Endarteritis obliterans from a cellular intimal thickening was present in 12 of the 100 cases, in high degree in only four, one the case of "primary pulmonary sclerosis" already mentioned, one a case of systemic hypertension, one a boy of 11 years with rheumatic carditis, and finally a woman of 77 with coronary disease and emphysema. Sometimes the bronchial arteries were involved by this process as well as the pulmonary arteries. In some of the patients the changes were definitely localized to areas of great pulmonary fibrosis or chronic pneumonia; in one case there were perivascular deposits of neoplasm. In only one of the 12 cases was there enough of this kind of pathology to cause any serious obstruction to the pulmonary circulation.

Hypertrophy of the media of the arteries was found in only two cases: the boy of 11 with "primary pulmonary sclerosis" and a woman of 33 with chronic nephritis and hypertension. Excessive muscularity of the large veins was found in several cases of heart disease and heart failure; in other cases it was infrequent.

Fibrosis of the media of the small pulmonary arteries was most frequent in the presence of lung and heart disease, especially when combined. Senility also seemed to be an important factor.

Syphilis of a pulmonary artery was found in only one case of the total group of 100 and here the lesion was most pronounced or perhaps localized in the artery to the middle lobe of the right lung. Based on this lesion there was a firm adherent thrombus. In seven of the 100 cases, including the one just cited above, the systemic arteries, in particular the aorta, showed evidence of luetic involvement.

There was no case of *aneurysm of the pulmonary artery* in the series. Such a lesion is exceedingly rare. We have never encountered one proved at postmortem examination with the exception of an instance during the World War of an arteriovenous aneurysm at the root of the right lung resulting from a gunshot wound. We have under observation two clinical cases with suspected aneurysm of the pulmonary artery.

Tuberculous involvement of the pulmonary vessels, veins as well as arteries, is invariably present in chronic pulmonary tuberculosis, affecting arteries or veins of any size although much more commonly the smaller vessels. Tuberculosis of the large elastic pulmonary arteries was found in only one of our cases and that showed caseation of the media up to the normal intima. Rupture of the vessel was evidently imminent and extensive hemorrhage through a fibrocaseous patch in the surrounding lung tissue would probably have resulted. It is such involvement of the pulmonary vessels which accounts for the frequent hemorrhages in phthisis. In several other cases of chronic pulmonary tuberculosis in the present series there were inflammatory changes in the smaller vessels. Endarteritis obliterans is the commonest lesion in the muscular arteries near tuberculous foci.

Rheumatism of the pulmonary vessels was found in two cases of the 100; one was a boy of 11 years who showed changes only in the chief veins, the other was a man of 39 with acute and chronic rheumatic heart disease who showed atheroma of the larger arteries and also diffuse thickening of the intima and endarteritis obliterans of smaller arteries. An adherent thrombus was present in the arterial branches to the right lower and middle lobes resulting in two infarcts in the right lower lobe.

Septic inflammation of the pulmonary vessels was encountered in several cases in the present series. Acute and subacute inflammations of the pulmonary vessels occur quite commonly and are usually not in themselves of great importance. The commonest cause is the lodging of septic emboli in the small, or more usually in the large, branches of the pulmonary artery. This may be followed by the formation of embolic pulmonary abscesses. A large pulmonary artery may be partly or completely blocked by a thrombus densely infiltrated by polymorphonuclear leukocytes with invasion of the underlying intima, media, and adventitia, especially of the media. A second important cause of septic inflammation of the pulmonary vessels is a chronic non-embolic lung abscess. In such cases it is especially the small veins near the abscess that are affected, both pulmonary and bronchial. Such changes in the small pulmonary veins make it easy to understand why secondary abscesses in the brain are so common in cases of pulmonary abscess.

The invasion of pulmonary vessels by *new growth* is common. It was found in six out of eight cases of neoplasm of the lungs in the present series. Sometimes the tumor in the lungs is confined to perivascular and peribronchial lymphatics and does not penetrate the blood vessels. When the arteries or veins are involved it is common to have in them a secondary endarteritis and thrombosis. In the cases studied in the present series the veins were more commonly involved than the arteries.

Thrombosis was next to sclerosis the most common abnormal finding in the 100 cases of the present study. It occurred in 27 per cent. In many cases there was an embolic origin but by no means in all. Arteries of all sizes were involved but in only one case was there any venous thrombosis. Thrombi visible to the naked eye were found in seven of the 27 cases and in four of these there were obvious sources of the embolism. The larger arteries were involved in nine cases and the smaller ones in 21. Organization of the thrombus in different stages was commonly seen. When the thrombus did not completely occlude the vessel, the earliest sign of organization was usually the proliferation of the intimal endothelium at the edges of the thrombus followed by a growth of endothelial cells over the surface of the mass and then by the ingrowth of new capillaries and fibroblasts into the thrombus from the underlying intima.

The three general conclusions to be drawn from this study may be stated as follows: (1) All pulmonary blood vessels are subject to a wide variety of pathological conditions, (2) sclerosis is as common in the pulmonary circulation as in the systemic, and (3) pathology of the pulmonary blood vessels seems to influence very infrequently either symptoms, signs, or the clinical course of disease.

A side-issue of this pathological study consisted in measurements of the thickness of the wall of the right ventricle as a guide to the amount of strain on that ventricle. A thickness of four millimeters or more was considered abnormally great. In 53 cases the right ventricle was found to be of normal thickness. Age per se had no influence, as would be expected. The majority of the cases with pulmonary disease had normal right ventricles but the great majority of those with heart disease or essential hypertension or both showed abnormally thick right ventricles. There was relatively little correlation between changes in the pulmonary vascular tree and thickness of the right ventricle except in the more marked cases.

A true *cor pulmonale* (or *pulmonary heart disease*) is distinctly rare, present in recognizable degree in certainly not much over one per cent of patients with heart disease. The case cited above of the boy eleven years old with the primary pulmonary sclerosis of unknown cause is a good example; his right ventricular wall measured 15 millimeters in thickness as compared with the normal left ventricle whose wall measured 9 to 12 millimeters; the heart as a whole weighed 305 grams, much too heavy for a boy of this age. He died of heart failure. Another striking instance of the cor pulmonale we encountered about two years ago at the Massachusetts General Hospital in a young man 29 years old with an extraordinary degree of silicosis from inhalation of dust in a gritty-soap factory. His right ventricle was found to be very large at postmortem examination while his left ventricle was normal. Aside from such infrequent and unusual cases, only occasional middle-aged and old people with chronic and very extensive pulmonary fibrosis, usually from infection, show the cor pulmonale. Ordinarily asthma, emphysema, and pulmonary tuberculosis, even though of high degree, do not produce the cor pulmonale.

Brief comment should be made in passing to obstruction to the pulmonary circulation either by direct pressure on larger vessels or more indirectly as the result of tumors and aortic aneurysms in the thorax or of chest deformities, especially extensive kyphoscoliosis. It is said that most kyphotic patients die eventually from heart failure. The strain is also said to be mainly on the right ventricle from obstruction to the pulmonary circulation but the systemic vessels and left ventricle may also be hampered by the deformity.

Involvement of the pulmonary arteries by embolism or thrombosis or both is a very common occurrence. If slight in degree it may produce little or no clinical manifestation in the way of symptoms or signs or influence on the health of the individual. As the study reported above shows, pulmonary thrombosis probably occurs in 25 per cent of all cases coming to autopsy; in most of these it is only of academic interest and undiagnosable, but when the process is a large one or very septic it may be important in itself. The most important effects are three in number: (1) the state of shock that may be induced by the vascular lesion, (2) the great increase in intrapulmonary blood pressure which may cause dilatation and failure of the right ventricle, and (3) the production of large infarcts in the lungs.

Pain, dyspnea, and collapse or any one or two of these three symptoms not infrequently ensue at once on the occurrence of pulmonary embolism and death may follow. The right ventricle may become dilated and insufficient.

Recently we have become interested in the syndrome of right ventricular embarrassment in cases of extensive pulmonary embolism. The heart is found to be laboring, usually with rapid regular rate and accentuation of the second pulmonary sound; in one case we heard to and fro murmurs over the pulmonary artery due either to dilatation of the valve ring or to close apposition of the engorged pulmonary artery to the chest wall; the cervical veins may be engorged and pulsating and the liver enlarged and tender; and in three recent postoperative cases we have found changes in the electrocardiogram which eventually may prove to be significant of this clinical condition; these were inversion of the QRS waves in Lead 3 (the so-called prominent Q_3) and inversion of the T_3 waves with somewhat high origin, slightly suggestive of one type of coronary thrombosis from which pulmonary embolism is sometimes differentiated with difficulty. In two of the three cases just mentioned the electrocardiogram returned to normal with clinical recovery and in the other case operation and autopsy proved the presence of extensive pulmonary embolism with dilatation of pulmonary artery and right ventricle and without coronary thrombosis. The careful analysis of history and such findings as those noted above along with the evidence later on of an area of pulmonary consolidation should help to distinguish pulmonary embolism from coronary thrombosis.

Pulmonary thrombosis is frequently based on pulmonary embolism but sometimes it arises in situ, developing on lesions of the pulmonary blood vessels themselves, especially favored by stasis in the pulmonary blood flow in cases of chronic heart disease and failure of high degree. It is not a rare complication of heart failure. Pulmonary hemorrhagic infarction when very extensive may cause jaundice, if the liver functions poorly as the result of congestion or infection; this accounts for a few instances of rather mysterious jaundice in cardiac patients with congestive failure without obstructing gall stones. Furthermore it should be added that pulmonary infarction may occasionally result from emboli coming from the right heart chambers, as when there is intracardiac thrombosis in the right ventricle over an infarcted area in

the interventricular septum or when there are infected thrombi on the tricuspid or pulmonary valve or on the ventricular or auricular endocardium or the pulmonary artery endothelium in cases of bacterial endocarditis complicating chronic heart disease, especially of congenital nature.

Finally, we would like to say a few words about *congestion or overfilling of the pulmonary circulation from heart disease.* There are three types: (1) The most common and important, is that due to failure of the left ventricle, acute or chronic, (2) also common and fairly important, is that due to deformity of the mitral valve, resulting in stenosis, regurgitation, or both, most characteristically stenosis, and (3) very rare and clinically unimportant, is that associated with dilatation of the pulmonary artery accompanying congenital lesions such as patency of the ductus arteriosus, an interauricular septal defect, or a triloculate heart with one ventricle and transposition of the great arteries. Little comment is necessary concerning the last two named conditions. We may simply note in passing that engorgement of the pulmonary circulation in mitral stenosis may be of high enough degree to cause pulmonary hemorrhage, or apoplexy as it is sometimes called, and periodically in rare cases to be suddenly increased by tachycardia to the point of calling forth a reflex of asthmatic breathing without failure of the left ventricle, a rare but definite type of cardiac asthma. In the congenital defects cited above the pulmonary circulation is much more active than the systemic circulation due to the short circuiting of much of the blood in the pulmonary tract.

It is, however, to the engorgement of the pulmonary circulation from failure of the left ventricle that we wish to call especial attention in closing. The condition is very common and yet often neglected. We look carefully for engorgement of the cervical veins, liver enlargement, and dependent edema without clearly realizing that in most cardiac cases, two thirds to three quarters of them, heart failure begins on the left side and often shows itself first through engorgement of the pulmonary blood vessels. Since this is so and since in a good many cases left ventricular failure, either in acute paroxysmal form, or in chronic low grade state, precedes right ventricular failure by days, weeks, months, or even longer, or is often preponderant when both ventricles fail, it behooves us to look sharply for pulmonary vascular congestion when we examine patients with the left ventricle under strain. In particular such cases are those with systemic hypertension, aortic valve disease, and coronary thrombosis (which is a condition that affects the left ventricle preponderantly). Dyspnea, cardiac asthma, pulmonary edema, reduced vital capacity, and visible engorgement of the pulmonary blood vessels by x-ray are the clues in these cases. Additional help comes from the finding of protodiastolic gallop rhythm, pulsus alternans, and accentuation of the pulmonary second sound where previously as in systemic hypertension the aortic second sound had been louder. Realization of the effect of weakness and failure of the left ventricle, clearly voiced by Hope 101 years ago, is, on a sounder basis, wisely being revived among us today.

PULMONARY EMBOLECTOMY*

BY ELLIOTT C. CUTLER, M.D.†

THE only reason for talking about pulmonary embolectomy at such a symposium is to apprize people that such an operation can be performed and that the only way to achieve success in cases for which this operation may bring relief is to be prepared at any moment for the procedure. We all know that pulmonary embolism is one of the most regrettable postoperative complications. It often strikes down one's most satisfactory case, often attacks youthful and otherwise perfectly healthy individuals. Obviously, its avoidance is more to be desired than its therapy and much has been accomplished in recent years to diminish the incidence of embolism through better technical surgical methods. The chief sources of the large emboli which concern us in a discussion of pulmonary embolectomy are the great veins in the pelvis, where, when clots form, no valves interrupt their course to the heart and lungs.

The operation for removal of clots from the pulmonary artery was first proposed by Trendelenburg in 1908. The first successful case was by Kirschner in 1924. The interval between the suggestion that the operation might be done and its successful completion is in line with many surgical innovations and perhaps it is well to call the attention of this gathering to this fact, for other procedures have been proposed for cardiac conditions which have not as yet been proved of much clinical value, but which later on may prove to be desirable remedial measures. Kirschner's first case was alive and well with normal electrocardiographic studies four years later. About thirty cases have appeared in the literature, though probably a great many more have been done and not published. Fourteen patients in all have survived operation and ten lived for a considerable period of time following the ordeal, though two of these later died, one twenty-five days following recovery with a recurrent embolus, and the other a short while later.

My own resident surgeons have done four

*Read at the meeting of the New England Heart Association at Boston, April 5, 1933.

†Cutler — Surgeon-in-Chief, Peter Bent Brigham Hospital. For record and address of author see "This Week's Issue," page 1298.

cases. None have survived, however, longer than a few hours. All, I am convinced, were operated upon too late following the observation of symptoms and signs which seemed to indicate that pulmonary embolism was occurring. In one of these cases, the patient was kept in the operating room eight hours, making sure that massive embolism was present before the operation was started. In this case a clot 25 cm. long was removed, but the condition of the patient was so grave that recovery did not occur. This small experience has convinced me that the dictum heretofore suggested that one should be sure the patient was dying before operating has not had a desirable influence. I see no reason why the modern surgeon should not operate, or at least expose the pulmonary artery, on early provocation rather than wait until a fatality is almost certain. A few negative explorations should do no harm and the successful cases will, under such circumstances, prove more numerous.

The operation, as you will see from the slides which will now be shown, is not very difficult. One makes a four or five-inch incision at the left border of the sternum, removing the second, third and perhaps fourth costal cartilage. The pleura is then pushed to one side and the pericardium opened. The sound is at once introduced into the great sinus, lifting the aorta and pulmonary artery, the catheter is attached to the sound, and these viscera pulled into the wound. The pulmonary artery lies most anteriorly, can be rapidly opened when thus strangulated without loss of blood, and the special forceps may be introduced into the right and left pulmonary arteries to remove the clot. Suction may be of further assistance in removing the smaller fragments of clot. The special suture-clamp can then be applied and suture carried out while the circulation takes place through the somewhat diminished caliber of the pulmonary artery. It has been said that the total circulation should not be shut off longer perhaps than one hundred seconds. In Nystrom's case it was discontinued for one hundred and four seconds so that probably two minutes may be utilized during total cessation of circulation. If too long a period is utilized, the anoxemia will seriously affect the brain cells, in addition to hurting the action of the heart itself. In assisting in the recovery of the heart, gentle massage and the use of adrenalin, both in the pericardial cavities and in the intracardiac cavities themselves, may be of value. Closure of the rest of the wound should be simple.

The critical matter in this whole affair seems to lie in full preparation for this operative ordeal at any moment. A complete set of instruments must be kept sterilized and prepared. The resident staff of all large hospitals should be trained to perform this procedure, for delay is fatal and any good young surgeon who has had five or six years of competent training and is familiar with this technique can perform this operation as well as more experienced surgeons. Time is the chief factor and when hospitals are fully prepared to carry out this ordeal, more satisfactory results will accrue.

DISCUSSION OF PAPER ON PULMONARY EMBOLISM BY DR. ELLIOTT C. CUTLER

BY JAMES C. WHITE, M.D.

In discussing such a radical new procedure as pulmonary embolectomy, it may be worth while to bring out another point of view which differs rather fundamentally from the one just presented by Dr. Cutler. At the Massachusetts General Hospital, Dr. Edward D. Churchill and I were given the assignment to operate on cases of pulmonary embolism in 1930. Since that time we have had the opportunity of removing clots from the pulmonary artery in seven cases. In three of these the heart had already stopped at the time the clots were removed, and neither by the use of adrenalin nor cardiac massage were we able to start up its beat. In two cases, however, the heart was beating feebly at the time the emboli were removed and vigorous contractions were restored after the pulmonary artery was cleared of its obstruction. In both instances, however, the delicate nerve cells in the respiratory centre had been deprived of oxygen for too long a time and the patients died of anemia of the medulla.

We differ from Dr. Cutler's statement in two ways. We feel first that it is not always easy to make a correct diagnosis. In one of the cases reported in the European literature, the operation was performed and no emboli were found; at autopsy it was discovered that the patient died of uremia. From our point of view the greatest difficulty lies in differentiating pulmonary embolism and coronary occlusion. In both conditions collapse may come on with startling suddenness; the fall in blood pressure, color of the patient, coldness of the extremities, and weakness of the pulse may all be similar. In one patient observed with a non-fatal pulmonary embolus, the finding of the electrocardiogram could have easily been mistaken for coronary thrombosis. I believe, however, that when a patient goes into sudden collapse during the first two weeks after operation and develops extreme cyanosis with weakening pulse, rapidly falling blood pressure and, most important diagnostic sign of all, extreme distention of his peripheral veins, he should be prepared for immediate operation. Even under these circumstances, I have watched a patient whose systolic blood pressure was reduced to 70, seen the blood pressure slowly return, and the patient get well spontaneously. All this makes us feel very definitely that we should not explore a doubtful case to establish the diagnosis. It is also the consensus of the surgeons of the staff of the Massachusetts General Hospital that operation on these cases should not be entrusted to the resident surgeons.

Dr. Cutler has told you that he considers this operation as being without great technical difficulty. I should like to take issue with this point also. It is extremely easy to open the left pleural cavity in the necessarily rapid removal of the ribs, and in certain cases both pleural cavities can be opened through an incision to the left side of the sternum. Nystrom, who has had an extended experience with the operation, admits opening the aorta instead of the pulmonary artery in one of his cases. The operation, to stand any chance of succeeding, must be done with the greatest speed and smoothness. Furthermore, one is forced to do a radical operation without the consent of the patient or of any member of his family. This may easily lead to legal difficulties. It is these considerations that have led the surgical staff of the Massachusetts General Hospital to regard this procedure as one involving important diagnostic, technical, and legal problems.

TYPES OF EDEMA AND THEIR TREATMENT*

BY HENRY A. CHRISTIAN, M.D.†

EDEMA, broadly speaking, is an accumulation of fluid in the tissues of the body, chiefly but not solely in the intercellular spaces. It may be a local or a general process. When, as a general process, it appears widely, almost universally distributed, we speak of edema as anasarca. The dominating constituent of edema fluid, so far as bulk is concerned, is water.

Edema results from a disturbed balance between the outflow of fluid from the vascular system into the tissues and the inflow of fluid into the vascular and lymphatic systems from the tissues, as a result of which fluid arrives in the tissues faster than it drains out of the tissues. Back of this lies a necessary relationship between fluid intake into the body and fluid output from the body. There is a normal optimal amount of tissue fluid with a considerable variation, which is considered normal; within these limits fluctuations occur from hour to hour; for tissue fluid to decrease or increase beyond certain limits is abnormal, the former constituting dehydration, the latter edema. A very considerable increase in tissue fluid must take place before it is demonstrable by simple clinical methods other than increase in weight, the latter occurring when the process is at all widely distributed even when otherwise the fluid increase is not demonstrable by the clinician. In ordinary clinical usage, until fluid excess is readily demonstrable in the tissues, we do not speak of it as edema. It is of edema in this sense that I will speak today, discussing chiefly general rather than local edema, confining my remarks to subcutaneous edema and the accumulation of fluid in body cavities.

When a patient appears, who shows edema, the problem presented is to find out the cause of this departure from normal. Since the maintenance of fluid balance in the tissues is a complex process, varied abnormalities in body function as regards fluid balance may cause edema. Consequently edema found in a patient may be an index of various abnormal or pathological conditions of function or structure, often of both. The problem is for the clinician to determine the cause of the appearance of edema in his patient as a logical step toward proper therapeutic management. If the cause of the edema is not made out, the probability is that a proper plan of treatment will not be developed, inasmuch as the removal of the edema will depend on correcting, so far as is possible, the underlying cause of the particular type of edema that the particular patient has. It is helpful to the clinician to have in mind some simple schema of the common causes or types of edema. The following I have found useful in my own clinical work.

- Circulatory failure edema
  - cardiac
  - hepatic
- Renal edema
  - of acute nephritis
  - of renal protein loss
- Nutritional edema
  - of plasma protein deficiency
    - albuminuria
    - diarrhea
    - starvation
    - unbalanced diet
    - anemia
  - of abnormality of plasma protein formation
- Inflammatory edema
- Anaphylactic edema
- Obstructional edema
  - venous
  - lymphatic
- Myxedema
- Endocrinal edema other than myxedema

A schema of this sort brings to mind the chief disturbances that cause edema and helps the clinician to work out the problem of cause in the individual patient. In many patients more than a single cause is operative, and there is a considerable overlap in the stated subdivisions in the schema. In other words the schema is merely a more or less crude summary of existing knowledge of edema and is in no sense an attempt at a scientific classification or explanation of the mechanism of edema.

Three important causes are effective in producing edema, (1) changes in pressure within vessels, (2) changes in the composition of plasma and body fluids influencing osmotic pressure, and (3) changes in the permeability of the walls of vessels. In some edemas endocrine control plays an important part. Besides water, the most important varying constituents of blood plasma and body fluids concerned in the production of edema are protein, particularly the relative amounts of albumin and globulin, and sodium chloride.

In studying the patient with edema, perhaps it is best to consider first the possibility of the edema being the result of circulatory failure of cardiac origin, since this is by far the most frequently occurring type of edema. Usually it is easy to determine whether this is the source of the edema. The patient gives a characteristic story of shortness of breath preceding the appearance of the edema, and physical examination shows definite evidence of a well-marked cardiac lesion; almost always cardiac hypertrophy is readily demonstrable. The distribution of edema is in large part determined by gravity. Edema of the face is infrequent. Ascites and hydrothorax often are found. Changes

*Read at the meeting of the Inter-State Postgraduate Medical Association of North America at Cleveland, October 20, 1933.

†Christian—Physician-in-Chief, Peter Bent Brigham Hospital. For record and address of author see "This Week's Issue," page 1298.

in filtration pressure within blood vessels is the chief cause of such edema.

There is a type of cardiac insufficiency with marked, generalized edema in which an incorrect diagnosis of nephritis with edema not infrequently is made. Often these patients give a history not suggestive of cardiac failure, and the appearance of widespread edema is almost the first disturbance noted by the patient. Very often the heart rate is little accelerated, and the rhythm usually is regular. Murmurs are absent except possibly an apical systolic one. Enlargement of the heart may be overlooked on physical examination. The most confusing evidences to many physicians are the findings on examination of the urine. It shows a very considerable albuminuria and numerous casts of varying types with not infrequent red blood and pus cells. It is a concentrated urine with elevated specific gravity. These findings tend to lead the physician to a diagnosis of nephritis and to attribute the edema to renal disease. If in doubt, the diagnosis may be settled by treating the patient as having cardiac insufficiency. Under a rest and digitalis régime the waterlogged condition disappears with surprising rapidity, and the urine clears largely of its evidences of renal disturbance, the changes in it having been caused by chronic passive congestion of the kidney. Few types of heart disease respond so dramatically to treatment as do these, and hence it is very important not to mistake them for some other type of edema and so fail to treat them as patients with cardiac insufficiency.

Patients with circulatory edema of cardiac origin, as a rule, give very satisfactory response to therapeutic measures appropriate to cardiac failure. Very often the edema will disappear without using any diuretic agent other than digitalis. Often its disappearance is expedited by a diuretic, and sometimes a diuretic is necessary. One of the xanthine diuretics, such as theobromine sodio-salicylate (diuretin) or theophyllin (theocin), usually is effective; failing a satisfactory diuresis from these, a mercurial diuretic, preferably salyrgan (mersalyl), almost always produces a marked diuresis. Diuretics, in patients of this type, are most effective when given after digitalis in adequate dosage has been given for 48 to 72 hours. Better results are obtained, as a rule, if the mercurial diuretic is preceded for several days by ammonium chloride, though this by no means is necessary for every patient.

Circulatory edema of hepatic origin, that is, edema resulting from portal obstruction, as a rule, is easily enough recognized, when that possibility is kept in mind, by having a history and physical examination suggestive of cirrhosis of the liver in a patient whose edema is dominantly an ascites and in whom the heart seems normal. Confusion may arise from forgetting that in numerous cases of cirrhosis of the liver the patient notes edema of his legs before observing any swelling of his abdomen. Later on the general edema in part results from protein loss from the blood into the ascitic fluid.

There is one form of cardiac disease in which ascites is such a dominating feature that the error of considering the cause to be hepatic is likely to occur. This is a cardiac insufficiency due to chronic obliterative pericarditis, a clinical entity sometimes known as Pick's disease. Surgery works such marked improvement in this type that its recognition is extremely important. Usually there is a past history of rheumatic fever. Murmurs are insignificant. Cardiac enlargement is present, but often not marked in degree. Fluoroscopic examination is of greatest aid in diagnosing the condition of the pericardium. The occurrence of this form of heart disease is very infrequent. This is unfortunate since surgical stripping of the thickened pericardium causes such striking improvement.

Circulatory edema of hepatic origin, chiefly ascites, is but poorly responsive to therapeutic measures. Digitalis is ineffectual. The mercurials are the only diuretics apt to produce a diuresis; often they fail. If so, mechanical removal of the fluid from the abdomen is the only recourse; this often must be repeated at short intervals to keep the patient comfortable. Surgery has been very disappointing in patients with cirrhosis of the liver.

In the study of the patient with edema, after having excluded circulatory failure in its various forms as the cause, it is best next to consider the possibility of a renal cause, since this is easily recognizable. There are two forms of renal edema (1) that associated with acute nephritis and (2) that due to protein loss in the urine and so usually associated with subacute or chronic renal disturbance. That it is a renal edema is suggested by the usual appearance of the edema in the face, especially around the eyes, where it is most marked on awakening in the morning. As a rule, the study of the urine makes evident the existence of nephritis.

The edema of acute nephritis seems to be caused largely, if not entirely, by a change in the walls of the blood vessels rather than by a change in the composition of the blood plasma or in circulatory filtration pressure. As a rule it is not marked or disturbing to the patient, disappears soon and requires no special treatment.

The other form of renal edema is caused chiefly by lowered osmotic pressure from decrease in the plasma protein, especially with a proportionate increase in globulin and decrease in albumin in the plasma. Almost always this type of edema is extensive; the tendency to its appearance in the face is a striking feature and

in contrast to the usual distribution of circulatory edema; still gravity does play a considerable part, too, in determining its distribution. The striking feature in the urine is the large amount of albumin. There is no evidence to be found of circulatory inefficiency. This form of renal edema is a variety of nutritional edema. Albumin loss through the urine is an important factor in its cause; to stop it would be the rational way of treatment, but unfortunately we know of no means to that end. Consequently treatment depends upon attempts to replace deficient protein in the blood plasma by feeding a diet rich in protein and upon removal of excess body fluid by diuretics and mechanical means. Mercurial diuretics and urea, the latter in large doses, are more effective than other diuretic measures. Digitalis is of no help. To restrict fluid intake and to lower the content of sodium chloride in the diet are therapeutic adjuvants. Treatment, however, is not very satisfactory. Diagnosis offers no great difficulty. The amounts of total plasma protein and of plasma albumin and globulin, with their lowered values, are quite characteristic; the edema fluid itself contains very minute quantities of these substances, less than in almost any other form of edema fluid. Determinations of these are of value, though not needed, except rarely, to make a diagnosis.

The form of renal edema, just described, is very closely related to the other types of nutritional edema in all respects except for the evidences of renal disturbance. Like protein loss through the kidney, protein loss through the bowel wall may occur in prolonged diarrhea and edema result.

A demonstrable, severe anemia with good renal function as determined by estimations of blood urea or phthalein excretion makes evident that edema in a given patient is caused by anemia and will disappear when treatment restores the blood to more normal values. Consequently a blood study should be a part of the method of examination of a patient showing edema.

Starvation edema is readily recognized as probable when there is a history of prolonged food deficiency. Its treatment is obvious when the cause of the edema is recognized. Plasma protein deficiency is an important factor in the mechanism of starvation edema.

Edema resulting from an unbalanced diet is not so easily recognized unless the possibility is kept in mind, and this source particularly sought for. Edema entirely due to such cause is rarely seen in the United States. Beri-beri, however, is a cause of such an edema, common in other parts of the world. It is, however, probable that vitamin lack or other type of food deficiency may be a fairly frequent partial cause of edema attributed to other factors. It is to be remembered that even though these food factors are ingested, they may not be absorbed or utilized. Further investigation may throw light on these relationships and elucidate edema so far not well understood.

There are seen occasional patients with edema resembling renal or nutritional edema in whom there is no albuminuria, no anemia and no discoverable food lack or food deficiency. Such patients show a low plasma albumin and high plasma globulin. Some have in the plasma large amounts of protein different from, though related to, the usual type of plasma globulin. Very little indeed is known about the mechanism of such abnormal plasma protein formation; these cases are grouped in the schema I have suggested as nutritional edema due to abnormality of plasma protein formation. Such a condition may appear in patients with multiple myelomata without edema or with edema. Recently I have studied a patient with edema of this general type but without evidence of bone tumor after extensive x-ray examination. What caused the low plasma albumin and high plasma globulin in this patient we were unable to determine. Until we know more of the process of formation and storage of body proteins, these various types of nutritional edema, especially the last, will remain incompletely understood.

Inflammatory and anaphylactic edemas rarely are difficult of recognition; their treatment depends on recognition of their cause. Here vessel walls undergo changes allowing of an abnormally free passage of fluid through them. Anaphylactic edema of various viscera may cause a great variety of symptoms and be difficult of recognition. These will not be discussed, since today we are concerned only with subcutaneous edema and accumulation of fluid in the body cavities.

Obstructional edema needs to be kept in mind as a possible explanation in patients seeking treatment of edema. Most often this form of edema involves the lower extremities, much less frequently the upper. However, as a result of obstruction of the thoracic duct ascites and hydrothorax may occur, as a rule of chylous type, i.e., containing fine droplets of fat in suspension, and this possibility should be kept in mind. Chylous fluids are simulated by the cloudy fluids, caused by high content of cholesterol, frequently encountered in one form of renal edema and in nutritional edemas, and this may cause confusion in diagnosis. Such pseudochylous fluids occur far more frequently than do truly chylous ones.

Venous thrombosis, particularly of the great veins of the pelvis and leg, is a frequent cause of edema of the lower extremity. Usually, though by no means always, there is a history to indicate the time and the cause of occurrence of the thrombus from which the condition has resulted. At times lymphangitis of the sheath of the vessels, both arteries and veins, seems an

important part of the process. Elephantiasis, both parasitic and non-parasitic, is met with causing a brawny swelling or chronic edema of the legs and may be difficult of diagnosis. Particularly interesting are those cases in which there are recurrent acute disturbances with local evidences of inflammation and general disturbances such as malaise and fever. A familial type of this is known as Milroy's disease, although not all patients with Milroy's disease have febrile attacks, and similar febrile attacks occur also in parasitic elephantiasis, that due to infestation with filarial organisms. In some patients there seems to be an admixture of venous thrombosis and chronic lymphangitis. In patients of these types chronic leg ulcers may develop and many of the patients have pronated feet. Very little really is known about the etiology and mechanism of these cases.

In some patients who have had venous thrombosis, there occur curious outbreaks of edema, the cause of which is not clear. In some of these patients, for example, very hot weather is productive of a marked degree of soft edema. In others a long time in one position without movement of the legs seems the cause. It is the possibility of bizarre developments of swelling and of edema that arouses particular clinical interest in the group of obstructional edemas and at times renders difficult the diagnosis of the condition. Treatment of most of the types of obstructional edema is surgical rather than medical. In many no form of therapy known at present seems to do any good.

Myxedema is well understood as to etiology and easily enough recognized by the general clinical condition of the patient; in cases of doubt a determination of basal metabolism by its very low figure fixes the diagnosis. However, the mechanism of edema in thyroid deficiency is but very poorly understood. It is not the result of circulatory failure nor of renal insufficiency; though moderately anemic, the anemia is not marked enough to cause edema. Certainly there is no element of venous or lymphatic obstruction and neither inflammation nor anaphylaxis plays any causative rôle. Plasma protein deficiency, though sometimes present, apparently is insufficient to be a cause of edema. No abnormal plasma protein constituents have been demonstrated. The edema fluid, as well as that accumulating in body cavities, has a very high content of protein, higher than in any other form of edema, being in sharp contrast to the very low content in renal and nutritional edema and being approached only by the fluid accumulated in patients with circulatory failure. This may cause the edema by increasing the osmotic tension of body fluid; but the cause of the increased protein in the body fluid is not known. In the edema of myxedema, therapy is very simple; properly adjusted thyroid dosage speedily clears it up, unless it has more than one cause such as a coincident cardiac insufficiency.

In connection with myxedema it is worth keeping in mind that Homans has noted swollen legs in young girls with lowered metabolism but apparently without myxedema.

Another rare form of generalized edema has just been reported by Thomas; it is cyclic occurring only at the menstrual period; there were no evidences of disturbed renal function and the blood showed no chemical changes except for a general concentration of all constituents. Here a relation to another endocrine function other than that of the thyroid in myxedema is suggested. It was found that the edema could be controlled by using a purified form of anterior pituitary-like sex hormone isolated from the urine of a pregnant woman. The importance of the two cases of this type of edema reported by Thomas lies in the indication of another endocrine relation to the mechanism of certain forms of edema, a relationship, which on further study, may prove to be more widely implicated in the mechanism of edema than had been supposed.

SUMMARY

Edema as seen clinically is of a varied and complex mechanism, in part only well understood. A knowledge of the varieties of edema in relation to their mechanism is helpful in the therapeutic management of patients with edema.

A CASE OF GASTRIC SYPHILIS SIMULATING CARCINOMA OF STOMACH*

BY BORIS KAPLAN, M.D.†

SYPHILITIC lesions of the stomach are rare and occur in the tertiary period, i.e., from two to 40 years after chancre. Pater[1] observed several cases of gastric syphilis in the secondary stage, but these are clinical manifestations and have never been proved anatomically. It is very possible that the roseola and papula syphilitica extend to the mucosa of the stomach and that syphilitic gastritis occurs due to local lesions, or to general syphilitic toxemia. But all these manifestations are entirely functional and disappear rapidly after instituting specific treatment. The history of gastric syphilis is comparatively a recent one. About a century ago Andral[2] was the first to recognize gastric syphilis and treated it successfully with mercury.

*Read at the Associate Staff Meeting at St. Luke's Hospital, November 15, 1932.

†Kaplan—Assistant Visiting Physician, St. Luke's Hospital, New Bedford. For record and address of author see "This Week's Issue," page 1298.

Topinard[3] in 1865 and Dujardin-Beaumetz[4] in 1866 reported cases with uncontrollable vomiting and hematemesis, which recovered on potassium iodide treatment. An autopsy performed by Lancereaux[5] on a man who died at the age of 66 years at the Hotel-Dieu in September, 1863, revealed among other luetic manifestations a syphilitic lesion in the stomach. Fauvel[6] demonstrated a syphilitic lesion in a woman's stomach. The researches of Virchow and the above authors stimulated the interest in this fascinating disease and a series of works appeared by the following: Fournier[7], Hayem[8], Chiari[9], Hemmeter[10], Einhorn[11], Dieulafoy[12], Bensaude[13].

Eusterman[14], divides the history of gastric syphilis into three periods. In the first, from 1891 to 1905, the diagnosis was based on postmortem material. During the second period, from 1905 to 1910, the diagnosis was obtained from clinical evidence and therapeutic test. During the third, from 1910 to the present time, the diagnosis has been based on x-ray, serology, clinical history and response to antiluetic treatment.

There has always been a controversy between the pathologist and the clinician on the question of gastric syphilis. The pathologist required first, a histologic section and later, with the discovery of Treponema pallidum, insisted on demonstrating this spirochete in sections. So far only two investigators have fulfilled this requirement—Warthin[15] and McNee[16]. The latter demonstrated a section of a chronic gastric ulcer with spirochetes in its walls at the Royal Society of Medicine. Clinicians, on the other hand, state that histopathologic studies are but rarely possible, since the treatment of gastric syphilis is essentially a medical one. They claim, according to McCann and Dumphy[17], that it is no more necessary to demonstrate the organism in stomach lesions than in syphilitic lesions of other organs.

Statistics. Osler[18] says that syphilis of the stomach is excessively rare. Eusterman[19] and O'Leary[20], from among 25,000 luetics, registered 93 cases of gastric syphilis. In Russia, where the sanitary conditions are poor, the incidence of gastric syphilis, according to Hausmann[21] and Luria[22], seems to be high. A. S. Merrill[23] in 1924 reviewed the cases at the Massachusetts General Hospital and found ten cases in 18,000 gastric examinations. Chiari and Stolper[24] examining systematically stomachs of syphilitics postmortem found tertiary lesions approximately 1:80. Pater[25] in 1907 collected 122 cases from the literature, of which 59 were proved histologically. Turnbull[26] at the London Hospital found one doubtful case in 3000 autopsies.

Occurrence. The disease occurs more often in men than in women. As Mathieu[27] remarks, this predominance is not only in relation to syphilis but also in relation to ulcer and cancer of the stomach. Excessive food, alcoholism and tobacco explain the fact. While gastric syphilis occurs in all ages, the greatest incidence is between 20 and 30 years.

Pathology. The syphilitic lesion, the gumma, is localized in the submucosa of the stomach, circumscribed or in diffuse form. The lesion consists of dense connective tissue-bearing collections of lymphoid and giant cells. It deposits in concentric layers around and in the walls of small blood vessels-veins and especially arterioles, so that an obliterative form of endarteritis results, which by diminishing the normal blood supply increases the tendency to necrosis. The obliterative endarteritis and the perithelial lymphocytic infiltration are the most characteristic features of syphilitic tissue. Syphilis may appear in different forms: 1) syphilitic ulcer, 2) syphilitic tumor, 3) syphilitic stenosis of pylorus, 4) syphilitic cirrhosis, 5) syphilitic gastritis, 6) gastropathie par radiculites syphilitiques, described by Bouchut[28], and later by Lamy[29].

Symptomatology. The symptoms are a reflection, more or less, of the underlying pathology. They may express themselves in the form of a dyspepsia, resemble a simple ulcer, or simulate gastric carcinoma, especially if it happens in the cancer age.

In the linitis plastica form the symptoms are variable.

In the gastralgic form pain is the most prominent symptom. It is very characteristic of Bouchut's radiculitis syphilitica. In the stenosis form the symptoms are according to the seat of stenosis: cardia, pylorus, hour-glass stomach.

I am presenting a case of syphilis of the stomach simulating gastric carcinoma which was admitted to the Clinic of St. Luke's Hospital, New Bedford, Massachusetts, on July 17, 1929, and which I had the opportunity to observe for over three years.

History.—A German woman, housewife, 37 years old, entered the Out-patient Department of St. Luke's Hospital because of pain in the epigastrium of six months' duration.

F. H.—Negative.

M. H.—She has been married 18 years and has two children who are apparently healthy. There has been one miscarriage. Her husband is living. His blood has a strongly positive Wassermann, but he did not admit a syphilitic infection.

P. H.—The patient had measles at the age of seven, frequent colds, nose-bleeds and a throat abscess in childhood. About six years ago she had her teeth extracted because of pyorrhea. She started to menstruate at the age of 14, and has always been regular. Her nervous and locomotor systems are normal. Her cutaneous system has always been normal. She does not remember any skin eruptions, except measles.

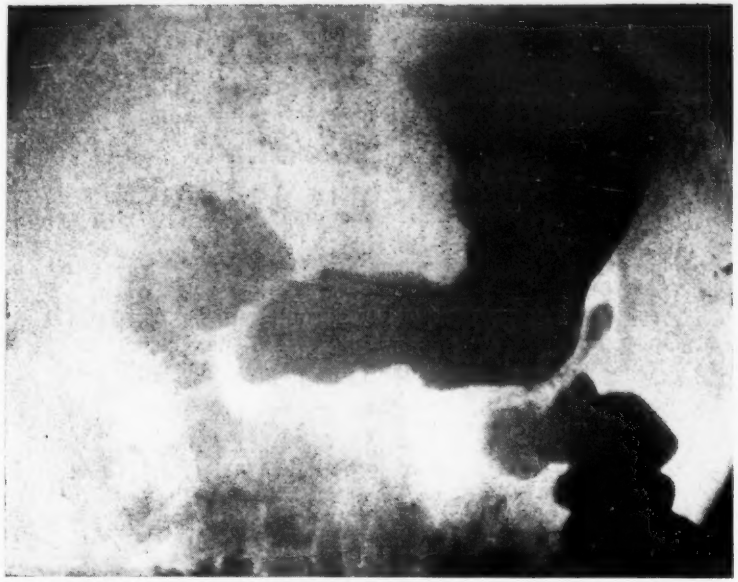

FIGURE I shows the original x-ray examination of Mrs. C. taken July 18, 1929. At this time there was a filling defect near the most dependent portion of the greater curvature. This was about 3.5 cm. in extent and 1 cm. deep. There was a palpable mass in this location and no peristalsis passed over the area.

FIGURE II shows result of examination on July 22, 1929 which corroborated the previous findings.

FIGURE III shows the condition of the stomach on October 20, 1930, following treatment. At this time the filling defect had entirely disappeared. No mass could be felt and peristalsis was normal.

FIGURE IV shows the result of the final x-ray examination November 3, 1932. At that time the stomach was free from any abnormality.

Gastrointestinal History.—Up to five or six years ago she had never had any gastrointestinal trouble except constipation. She then began to have occasional attacks of vomiting in the morning, not associated with abdominal pain or loss of appetite. She always slept well up to the past six or seven months. She never rests during the day. She does not use alcohol, tobacco or drugs. She has three meals a day, is very fond of coffee, occasionally drinks tea, and uses a moderate quantity of condiments: pepper, salt, vinegar, and mustard. She takes no exercise. She has never been jaundiced. She has never noticed any mucous, bloody, clay-colored or tarry stools.

Present Illness.—It started about six months ago with nausea and vomiting shortly after meals. The vomitus consisted of acid fluid and food. There was no bile, blood or food of the previous day; the color was never a coffee brown. The vomiting is not easy but occurs with great exertion. Only once, about six weeks ago, she vomited some blood. Every kind of solid or liquid food brought on abdominal distress and vomiting.

The vomiting is associated with a more or less dull continuous pain in the epigastrium radiating to her back. The pain always stays in the epigastrium, increasing in severity before meal times and at night and is not relieved by food or soda, only hot tea occasionally relieving it. Her appetite is fair; she is not thirsty. Her taste is normal. Her deglutition is normal. She has no heartburn. She belches occasionally with no foul odor. Six months ago after the onset of the pain she consulted a physician who diagnosed ulcer and gave a diet of milk, cream, cereals and powders without relief. Another physician prescribed small white pills and powders; the pills gave her a little relief, but in spite of the diets and medication, the disease progressed and she lost about ten pounds.

Physical Examination.—The patient was a thin emaciated woman, with pale mucous membrane. Head—Normal. Eyes—Pupils equal, react to light and accommodation. Mouth—Teeth out; tongue slightly coated, no soreness, no atrophy of papillae, or tremor. Cervical and other superficial lymphatic glands are not enlarged. Thyroid enlarged (a firm nodule was located in the right lobe). Heart and lungs normal. Abdomen—The abdominal wall is flabby. There is a diastasis of the recti muscles. The liver is about 3 cm. below the right costal margin. The spleen is not palpated. About 2 cm. above the umbilicus is felt a tender mass, of hard consistency. The flabbiness of the abdominal wall together with the diastasis recti makes palpation of the mass very easy and outlines its edge very distinctly above the umbilicus. Reflexes—Knee jerks are equal and active. Babinski negative.

Laboratory.—The urine is negative. Hemoglobin 50%. Red blood cells 3,800,000. White blood cells 9,600, Polys 79%, Lymphocytes, 18%. Repeated Kahn and Wassermann positive. Gastric analysis: free HCL. absent with ½ mg. histamine. Stool—Guaiac negative.

Roentgen—The stomach is normal in position, size, tone and shape. There is a filling defect near the most dependent portion of the greater curvature, irregular in outline, about 3.5 cm. in extent and 1 cm. deep. There was a palpable mass in this location and no peristalsis was observed passing this point. The patient complained of tenderness directly over the mass. The sphincter is negative and the duodenal cap normal. In six hours the barium reaches the hepatic flexure, in 12 hours the splenic flexure, in 24 hours the rectum. Probably gastric malignancy. (Dr. James M. Bonnar.)

Treatment.—Bearing in mind that this woman never kept a regular dietary régime, she was placed purely from a diagnostic point of view on a Sippy diet. She stopped vomiting, but the pains did not disappear. Then she was started on specific treatment with intravenous injections of 0.3-0.45 neoarsphenamine and intramuscular injections of quinineiodobismuthate. Between the courses she has been taking potassium iodide. After the first three weeks she showed great improvement. She stopped vomiting, her abdominal pains disappeared and at the end of six weeks she had gained eight pounds. First she was kept on a soft diet but later she ate the usual house food. The abdominal mass disappeared gradually within three months. X-ray examinations on October 15, 1930, showed no evidence of the previous lesion.

Patient's Present Condition.—She weighs 151 pounds (a gain of 25 pounds since July, 1929). Her general condition is good. X-ray examination reveals no lesions. Gastric analysis still shows absence of HCL with histamine. She still shows a positive blood Wassermann and a moderate secondary anemia. (Hemoglobin 65%.) There is no stomach trouble and no constipation.

Discussion.—The symptomatology here is so variable that the clinical picture is not characteristic of a common disease. First of all we shall think about cancer, but according to Lebert's and Smithies' statistics, it is rather rare to see a carcinoma of the stomach at the age of 37, especially in women. The patient is thin, her mucous membranes are pale, she is emaciated, but not cachectic and her appetite is fair. She lost only ten pounds, and only the existence of a tumor makes us think of a cancer belonging probably to the scirrhous type. But on the other hand, if this is malignancy, it is strange to see a combination of such grave anatomic changes of the stomach with comparatively good general appearance and with fair appetite. First it was thought to be a simple peptic ulcer, especially bearing in mind that her pains coincided with an empty stomach. But the absence of free HCL, even with histamine and the remarkable resistance to diet and alkalies. makes the diagnosis improbable. Among the rarer diseases of the stomach, lymphoblastoma should be considered. According to the literature it is very difficult to diagnose this disease in vivo. The blood picture is not much of a help here (Karl Sternberg[30]). As to the x-ray findings, they also are not sufficiently characteristic to permit of a specific diagnosis, but when taken with clinical findings, may be of considerable value (Holmes, Dresser, and Camp[31]). Junghagen[32] suggested that a strictured cuff-shaped area in the pyloric region might be specific for one stage of the disease. Ruggles and Stone[33] mention "the persistence of peristalsis in the presence of deformities" as characteristic of lymphoblastoma. All these signs are absent in the roentgen pictures of this case. The most striking clinical symptoms of lymphoblastoma (Hodgkin's type) are loss of weight, fever of the Pel-Ebstein type, diarrhea, pruritus. All these symptoms except loss of weight are also absent in this case, and even the loss of weight was observed only in the beginning, before the

FIGURE IV shows the result of the final x-ray examination November 3, 1932. At that time the stomach was free from any abnormality.

FIGURE III shows the condition of the stomach on October 20, 1930, following treatment. At this time the filling defect had entirely disappeared. No mass could be felt and peristalsis was normal.

antiluetic treatment was instituted. Finally, if this were a lymphoblastoma, the antisyphilitic treatment alone, without roentgentherapy, would not greatly improve the patient's condition, and iodine would even make her feel worse.

There are some benign tumors in the stomach that will cause a filling defect. Hair balls can cause such a defect, but never an absence of HCL; never a secondary anemia. There is one more disease which is quite rare, but which we have to consider here in view of the strongly positive Wassermann. This is gastric syphilis. The surprisingly extensive lesion as shown by x-ray, the comparatively good general appearance, the long and uncharacteristic history, the positive serologic test should make us think of gastric syphilis, especially when there is syphilis in her family (patient's husband). But two facts seem not to be in favor of the latter diagnosis. Our patient is a female and the literature states that gastric syphilis occurs twice as frequently in the male as in the female. The other fact which is rare for gastric syphilis, according to Einhorn, Eusterman and Moore, is the finding of a palpable mass. Therefore if this is gastric syphilis it would be a very rare case due to the foregoing facts. Having these in mind, the antisyphilitic treatment was started with some doubt in relation as to diagnosis. A positive Wassermann according to the literature is not so rare in cases of carcinoma of the stomach and may be absent in cases of gastric syphilis.

The patient responded to the treatment excellently. The pain and vomiting disappeared within three weeks and she gained in six weeks eight pounds. While this therapeutic test was certainly a great aid in diagnosing the case, the response to the specific treatment does not always mean that the lesion is necessarily syphilitic. Improvement of the general condition may follow after the use of such potent chemicals as arsenic, bismuth and iodine. On the other hand, the lesions may be sclerotic due to syphilis and of course will not be improved by specific treatment. Fournier made a remark about the contrast between luetics and cancer patients in relation to iodine: "While syphilities are greatly improved, cancer patients do not tolerate iodine." This patient between the courses of treatment with bismuth and arsenic received potassium iodide by mouth and seemed to tolerate the treatment very well.

Summarizing the facts: An unduly long and not characteristic history, a secondary anemia, an absence of free HCL, a combination of an extensive lesion as seen by x-ray with relatively good conservation of general health, an excellent response to antiluetic treatment and a good tolerance to iodine would indicate that we are dealing here with gastric lues.

Could it possibly be malignancy in spite of all enumerated facts? Every syphilitic may have a carcinoma or a lymphoblastoma at the same time, particularly cancer of the pylorus being not rare according to the literature. While it was difficult to answer the question in the beginning, the possibility should certainly be excluded now, in view of the continued good health of the patient for the past three years and eight months.

SUMMARY

A case of gastric syphilis with a palpable mass is reported in a woman of 37 with a parallel review of the literature.

If the incidence of gastric syphilis is rare, especially in women, it is still rarer when we consider the presence of a distinctly palpable tumor.

The diagnosis of gastric syphilis would not be so difficult provided one would bear in mind the possibility of this disease.

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OBSERVATIONS ON THE USE OF PARAFFIN OIL PREPARATIONS*

BY ROBERT L. PATTERSON, M.D.,† AND CHESTER M. JONES, M.D.†

IN the treatment of certain types of constipation it has become customary, during recent years, to make use of various preparations of paraffin oil, the purpose of which was to soften the dejecta and, by providing mechanical lubrication of the bowel, render more easy the passage of fecal material. The advantage of paraffin oil for such a purpose lies in the fact that it is not split by lipolytic enzymes and is not absorbed from the digestive tract. It has become recognized, however, that lubrication as such is not of primary importance and may not be desirable, but that soft bulk which would stimulate the bowel without undue irritation is what is chiefly needed.

Frequently, paraffin oil alone will not mix thoroughly with fecal material but is eliminated separately without facilitating the passage of the dejecta to any great degree. A further objection which is frequently raised to oil is that it may leak past the anal sphincter without producing a defecatory reflex.

To obviate such leakage and to provide a more physiological type of aid in the formation of a soft, bulky stool, attempts have been made to produce a permanent emulsion of paraffin oil in combination with some other non-irritating inert substance. Such a preparation might be expected to mix readily with the fecal material, giving a soft, bulky stool which would stimulate peristalsis without undue irritation.

In addition, the oil, by being in a permanent emulsion made up of oil droplets of uniform size, would remain in physical combination with the stool and would not tend to leak or be passed independently of the fecal material. The smaller the oil droplets, the more permanent would be the emulsion.

Two types of such preparations are at present available: one consists of a combination of paraffin oil and agar-agar; the other, of a combination of paraffin oil and Irish moss.

In order to add a slight laxative effect to such preparations, phenolphthalein is at times added in suitable dosage. In this brief study, we have attempted to observe the effects on the stools of paraffin oil alone, oil and agar-agar, and oil and Irish moss, when given by mouth. We have assumed that the most valuable and the most physiological results would be obtained by that preparation which mixed most thoroughly with the stool, thereby giving bulk and preventing leakage or loss of oil. If such an assumption is correct, the preparation providing the most perfect emulsion would be most easily miscible with the fecal material and should be identified in the stools as small fat globules of fairly uniform size.

*From the Medical Clinic of the Massachusetts General Hospital, Boston, Massachusetts.

We are indebted to the E. L. Patch Company, Stoneham, Massachusetts, for the materials used in this study.

†Patterson—Intern in Orthopedics, Children's Hospital, Boston. Jones—Physician, Massachusetts General Hospital. For records and addresses of authors see "This Week's Issue," page 1298.

METHODS OF OBSERVATION

In the following studies we have used the three preparations mentioned above on a group of hospital patients, giving a uniform daily dose of one tablespoonful for a period of several days, and then the stools were studied carefully. The results are described below. In several instances, each of the three preparations was given at different times to the same patient. In all, 102 stool specimens were studied as obtained from 19 patients. In addition, a few observations were made on the stools of patients who had received paraffin oil, agar-agar, and phenolphthalein mixture, or oil, Irish moss, and phenolphthalein.

Each stool was examined individually for leakage of oil and microscopically for the purpose of measuring the distribution and actual size of the oil droplets. By leakage is meant the oil present on the surface of the fecal material not thoroughly mixed with it, plus any gross oil present when the stool was passed into the container.

In order to determine the leakage of the oil, the following method was used. The feces were flooded with water (or 50 per cent alcohol when the feces were lighter than water) allowing the oil on the surface of the feces to rise to the top. The oil was decanted into a separatory funnel and flask. Excess water was drawn off and the oily layer on the sides of the flask plus the oil already collected were dissolved in ether. The flask was inverted and boiling water allowed to gravitate into the bottom of the flask. As the ether layer on top of the water gradually evaporated, all the oil remained at the top of the flask and from there was run into a calibrated tube and measured in cubic centimeters.

The observations on the state of emulsification of the oil as it was passed with the stool consisted in accurate measurement of the size of the fat droplets by means of a micrometer attachment on the eyepiece of a microscope. Measurements were in microns. At first the fat droplets of the stool specimens were stained with an alcoholic solution of Sudan IV, but later measurements were made on unstained specimens

inasmuch as the difference in the results obtained between the two methods was less than 0.7 microns. One hundred droplets were counted in each microscopic preparation. As stated above, it was felt that the stool specimens showing the smallest and most uniform oil droplets would present evidence of the most stable emulsion and the one least liable to gross oil leakage.

FINDINGS

The results of the above studies are outlined in the accompanying table. Of the 18 patients receiving plain paraffin oil, 13 showed leakage as defined above. The amount of such leakage varied from 0.02 cc. to 2.5 cc. per stool, with an average amount of free oil of 0.68 cc. The stools of five patients out of seven receiving a mixture of oil and agar-agar also showed leakage by the above test. The amounts obtained in individual specimens varied from 0.02 cc. to 0.6 cc. with an average amount of 0.35 cc. of free oil.

No patient receiving a mixture of Irish moss and oil showed any leakage as determined by the separation test described above. These figures are of comparative value inasmuch as seven of the patients received each of the three preparations on separate occasions and five others received both plain paraffin oil and the mixture containing paraffin oil and Irish moss.

As regards the size of the oil droplets in the stools, during the use of the three preparations, the results were similar to those just noted. In the 50 stools studied after the use of paraffin oil alone, there was very little uniformity in the size of the oil droplets, the micrometer measurements ranging between 10 and 180 microns. The average size of the droplets in all the specimens studied was 46 microns, with a variation for the individual stool specimens of from 25 microns to 90 microns.

In the case of 20 specimens obtained after the use of oil and agar-agar, there was greater uniformity in the size of the droplets which were much smaller than in the preceding group. In these specimens, the size of the droplets ranged between 6 and 80 microns, with an average diameter of 26 microns. The average diameter for 100 globules in the individual stools varied from 17 microns to 34 microns.

The 32 stools obtained after the use of oil and Irish moss showed the greatest uniformity in the size of the oil globules and also the smallest globules. The extreme variation in the diameter of the oil droplets lay between 6 and 40 microns, with an average diameter of 15 microns. The average diameter of the droplets in single stools varied between 9 and 19 microns.

In addition to the above observations, a few stools were examined following the use of oil and agar-agar, or oil and Irish moss, combined with phenolphthalein. The results listed in the table below are in accord with the preceding findings. Even with the more rapid intestinal rate brought with the action of a cathartic such as phenolphthalein, the leakage and the state of emulsification of the oil seemed to remain relatively unchanged in either of the preparations.

TABLE SHOWING SIZE OF OIL GLOBULES AND OIL LEAKAGE IN THE STOOLS OF PATIENTS RECEIVING VARIOUS OIL PREPARATIONS

Preparation employed	Number of patients	Number of stools examined	Average diameter of oil globules in feces	Largest size globule noted	Smallest size globule noted	Leakage of oil
Paraffin oil alone	18	50	45.9	160	10	0.02 cc. to 2.5 cc.
Oil and agar-agar	7	20	25.8	80	6	0.02 cc. to 0.6 cc.
Oil and Irish moss	13	32	15.0	40	6	0
Oil and agar-agar with phenolphthalein	2	2	22.2	60	8	0.05 cc.
Oil and Irish moss with phenolphthalein	3	4	21.7	42	8	0

CONCLUSIONS

1. From the above results, it would seem proper to conclude that gross leakage of oil is less likely to occur from the use of an oily emulsion of paraffin oil and Irish moss than from a similar emulsion of paraffin oil and agar-agar. Both preparations show less tendency to leakage than paraffin oil when used alone.
2. This decreased tendency to leakage is associated with a greater uniformity in the size of the oil globules and with a smaller actual diameter of the individual droplets.

STUDIES OF REPRODUCTION IN THE RAT*

IV. On The Occurrence of Spontaneous Amputation In Young Growing Rats Whose Mothers Were On Certain Diets

BY DONALD MACOMBER, M.D.†

DURING the course of the experiments previously reported in Parts I, II and III of this series a peculiar phenomenon was observed in the growing nurslings. This phenomenon at that time believed to be unique, was the development of annular constrictions close to the base of the tail. Sometimes these constrictions, which usually remained rather insignificant and caused little or no subsequent disturbance in the normal development of the tail, became deeper. In this case dry gangrene (figs. 1 and 2) with spontaneous amputation of the tail usually developed. Occasionally the amputation did not involve the entire tail distal to the constriction, but only the tip was lost. If this happened the remaining tail had a ringed and generally deformed appearance. Further search among the experimental colony disclosed many instances of tail amputation, and a number of cases in which one or more toes of the hind feet had undergone similar amputations.

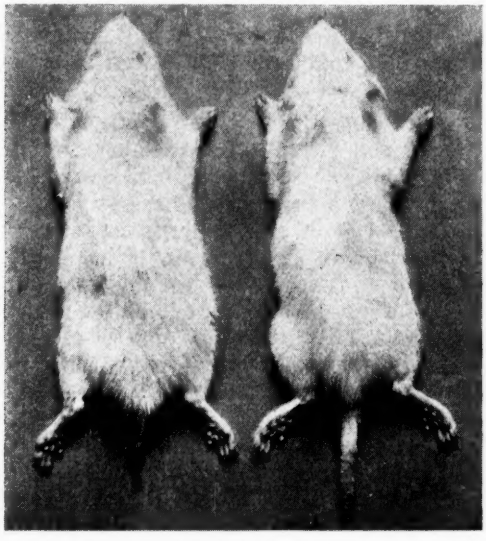

FIG. 1. This shows two partially grown rats; the one on the left with gangrene and partial amputation of tail and toes; the one on the right with knobbing and ringing of tail.

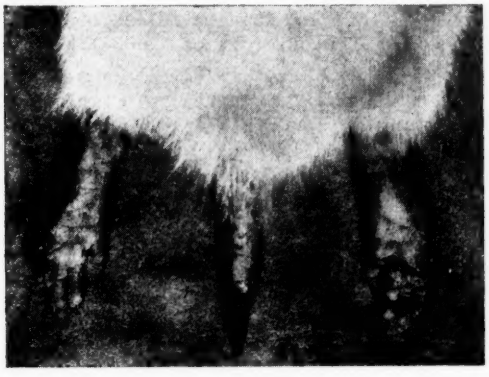

FIG. 2. Enlargement of the left-hand rat shown in Fig. 1. The amputation of the outer toes on both hind feet as well as that of the tail shows plainly.

The character of the amputations was so similar to that of the intra-uterine amputations sometimes found in human beings that the subject was brought to the attention of Dr. George L. Streeter[3], Director of the Carnegie Laboratory of Embryology in Baltimore. He was much interested and reported that the phenomenon was known to Drs. McCollum and Simmonds at Johns Hopkins, and had also been seen at the Wistar Institute. On the whole he considered it due to a germ plasm defect, feeling sure that it was not of infectious origin and being doubtful whether it could be attributed to some lack in the diet. He found only one instance in the literature in which a similar phenomenon had been reported. This was in 1927 when Zanadskaia[4] published a paper on spontaneous gangrene of the tail among mice and on the existence of an hereditary lethal factor. His mice had been treated with x-ray and subsequently gave birth to young which developed the tail gangrene. When these bobtailed mice were interbred, bobtails were produced in the proportion of 100 to 47 normals. This he interpreted to be similar to the experience with yellow coat color in mice where a lethal factor is thought to be associated with the factor for that coat color so that no mice homozygous for the character can be bred.

It had seemed to the author, however, that the amputations were much more likely to be due to some lack in the diet. With that in view he extended his experimental work in an attempt to prove the matter once and for all. The results were suggestive of the correctness of his views, but publication was postponed until more extensive observations were possible. There the matter stood until in 1931 Slonaker[2] published his work already quoted on the Effect of Different Percents of Protein in the Diet. On page 549 he makes the following statement: "After a short time it was found that the diet was deficient in Vitamin B. This was especially noted in the offspring of the animals on low protein, group I (protein 10.3 per cent) and was

*The experimental work upon which this paper is based was carried out in the Research Laboratory of the Department of Obstetrics, Harvard Medical School. It was aided by grants from the Delamar Fund.

†Macomber—Research Fellow in Obstetrics, Harvard Medical School. For record and address of author see "This Week's Issue," page 1298.

manifested by greatly retarded growth of the young and often by malformations. Such conditions were not observed in the other groups. The most common deformities consisted of blindness or of a loss of from one-fourth to three-fourths of the tail. This latter process followed a definite order. A constriction would appear about one-fourth of the length from the tip of the tail, the distal fourth would become very edematous, often increasing in diameter to four or five times the normal, and finally drop off. If the process continued, a second and finally a third quarter would be similarly disposed of, leaving bobtails with but a fourth of the tail remaining ——. We at once increased the amount of Vitamin B by adding Fleischmann's yeast especially prepared for stock and poultry. After this there were no more malformations and the mothers were better able to nurse the young." In view of this observation that certain diets could be responsible for the occurrence of a similar condition it seemed worth while to report the matter in full as it appeared in this series.

The stock used was of mixed genetic character. Of the 54 females used 35 were albino and 20 colored, while the colors of four were not recorded. The males were as follows: albino four, colored two, color unknown three. The tails of the offspring from 17 females showed actual amputation or such severe constrictions that the nutrition and development of the tails were seriously affected. Of these 17, six were colored and eleven were albino. The matings which produced the litters developing the bad lesions are shown in table 1.

TABLE 1

C (♂ 74) X C (♀ 1); A (♂ 72) X A (♀ 2); A (♂ 73) X A (♀ 2); C (♂ 72) X A (♀ 11);
A (♂ 71) X A (♀ 11); A (♂ 75) X C (♀ 12); A (♂ 71) X C (♀ 12); A (♂ 73) X A (♀ 13);
A (♂ 71) X C (♀ 19); A (♂ 75) X A (♀ 20); A (♂ 71) X A (♀ 26); A (♂ 73) X A (♀ 30);
C (♂ 74) X C (♀ 31); A (♂ 71) X C (♀ 31); C (♂ 74) X C (♀ 31);
C (♂ 74) X A (♀ 32); C (♂ 74) X A (♀ 32); C (♂ 72) X A (♀ 33); A (♂ 75) X C (♀ 34);
A (♂ 71) X A (♀ 35); A (♂ 71) X C (♀ 36); C (♂ 74) X A (♀ 37); C (♂ 72) X A (♀ 38).

From this it would appear that all five males were involved at one time or another; that the amputations appeared just as frequently when both parents were albino; and that if the same mother had two affected litters they might have been sired by different males. Subsequent matings of these same males and females on different diets failed to produce lesions except as noted below. The evidence would seem therefore extremely doubtful that any hereditary factor was here involved. This is strengthened by the fact that later matings of animals with amputated tails, while on normal diets during lactation, failed to produce further lesions, and that no second generation intermatings, even though of the same stock, yielded anything abnormal.

The dietetic origin is at least strongly suggested by the evidence which will now be brought forward. It is summarized in table 2.

This table is a summary of the records of 40 female rats and the lactations following (with the few exceptions noted) four pregnancies each. The "normal" diet group numbered 1-10 and 31-40 had 20 per cent protein with unlimited calories. The "experimental" diet group numbered 11-30 either had their protein restricted or their calories restricted during a portion of the observation. Apart from that, all 40 were submitted during pregnancy and lactation to the changes noted under "changes in character of diet." These changes concerned the amount of wheat germ and lettuce in the diet, either one or both of which had been introduced as a source of vitamin E (see Part III*).

Of the twenty rats (Nos. 1-10 and 31-40) on the normal protein and calories 10, or 50 per cent, had young developing severe lesions or amputations after four months on a diet containing wheat germ and no lettuce. Of the other twenty rats (Nos. 11-30) 7, or 35 per cent, had young with similar severe lesions. The probability therefore is that neither changes in protein nor calories played any significant rôle in etiology. The two groups may therefore be combined, giving an incidence of 17 out of 40, or roughly 42.5 per cent. This is very high indeed. It occurred, as has been stated, after four months of a diet containing wheat germ but no lettuce. It was cured in every instance except one by the introduction of lettuce, and the removing for 39 days of all wheat germ. After that it did not return even when the wheat germ was put back in the diet. Unfortunately it was impossible to continue a second period of wheat germ without lettuce for more than 45 days. During this period no further severe lesions were noted save in the case of the young of Rat 31—the one exception to the curative effect of the lettuce in the preceding period.

The evidence that lettuce adds something to the diet not found in the wheat germ is strengthened by the records from the previously reported work on calcium[1]. In that series† a very similar diet was used to the one employed in the present series except for the fact that no wheat germ was included and lettuce was given daily

*New Eng. J. Med. 209: 1235, 1933.

†NOTE: Casein 20, Salt. Mixt. 4, Starch 56, Lard 20. To this was added 0.2 Gm. yeast, 0.2 Gm. cod liver oil and 20 Gm. lettuce per rat per day.

TABLE 2

Date	Changes in Character of Diet	Rat no.	1-10 Prot. 20% Cal. unlimited		11-20 Prot. 20% Cal. restricted				21-30 Prot. low Cal. unlimited				31-40 Prot. 20% Cal. unlimited						
			1	2	11	12	13	19	20	26	30	31	32	33	34	35	36	37	38
10/11-2/14	5-10%	Rat no.	OK	X	X	X	X	OL	X	OK	X	X	OK	X	X	OK	OL	OK	OL
2/14-3/28	10%		X	X	X	X	OP	X	OK	X	OP	X	X	OP	OK	X	X	X	X
3/28-5/6	0		OK	OK	OP	OK	OK	OK	OK	OL	OK	X	X	OK	OK	OK	OK	OL	OK
5/6-6/20	10%		OK	OK	OK	OP	OK			OL	OK								
5/6-6/20	10%							OK	OK			X	OP	OK	OK	OK	OK	OK	OK

Note from 5/6-6/20
Rats 1-15 and 21-30 had lettuce
Rats 16-20 and 31-40 had no lettuce

OK = normal pregnancy and lactation
OP = not pregnant in this period
OL = normal pregnancy but no young survived
X = normal pregnancy and lactation with young showing severe lesions of tails or toes

throughout. In all, 25 complete pregnancy-lactations were observed,—10 on the control diet and 15 on the low calcium diet. In no instance did any lesions of tails or toes develop.

Just what the occurrence of spontaneous amputation on certain diets signifies it is as yet impossible to state. It seems fair to conclude either that there is some substance in lettuce, not present in wheat germ, which is necessary for the proper nourishment of nurslings, or that there is some toxic substance in wheat germ which can be transmitted to the young through the mother's milk which can, however, be neutralized by the addition of lettuce to the mother's diet. Slonaker[2] found the same thing and attributed it to a lack of vitamin B since it was cured by the addition of more brewer's yeast to the diet. His original diet contained, however, a considerable proportion (nearly 20 per cent) of whole wheat, and might also have contained therefore a toxic element from the wheat. The cure after adding yeast might be explained again as a neutralization.

In the case of Slonaker's work and that reported here, the fact that dietetic changes caused the condition to disappear would seem conclusive proof against any hereditary germ plasm defect.

SUMMARY

When mothers on a diet containing wheat germ and no lettuce, but otherwise adequate as regards protein, calories, mineral salts and vitamins A, B (B + G), D and E, were observed during complete reproductive cycles, it was found after an interval of four months that the young of more than 40 per cent developed severe lesions of the tails or toes, frequently leading to spontaneous amputation. A course of lettuce permitted 16 out of the 17 (94 per cent) mothers whose young had been affected to rear normal litters. It is suggested that there is some toxic substance in wheat (or wheat germ) which produces this condition, or that some nutritional substance necessary for the normal growth of nurslings is present in lettuce but not in wheat germ. The subject would seem to warrant further investigation and study.

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AMOEBIC ABSCESS OF THE LIVER WITHOUT PRECEDING DIARRHEA

CASE REPORT

BY LELAND S. MC KITTRICK, M.D.*

G. H., aged 55 years, was seen at his home, Brookline, Mass., on December 4, 1933 at the request of Dr. S. F. McKeen. He presented the following letter from an excellent surgeon in a well known medical center, dated November 25, 1933.

> "—— Mr. H— has had a long serious illness dating from about July 28th of this year. He was seen at that time by an excellent physician, Dr. F—. He had an acute illness with high fever and this was followed in a few days with slight friction rub over the lower right pleural region. Dr. F— believed at that time that he had an influenza infection. About five days after the onset of this illness he developed pain and tenderness over his gall bladder region accompanied by nausea and vomiting. A few days later he developed pain and tenderness over his lower right abdominal region and it was at this stage of his illness that I saw Mr. H—. That was on August 9th. On this day he had very definite tenderness over his appendix, marked muscular rigidity and a continuance of his temperature of about 101 degrees. When I saw him, this condition was of about 48 hours' duration. I may add that an x-ray at this time showed evidence of some trouble in his lower right lung, probably incomplete resolution of a pneumonic process. He had a marked increase in his liver shadow on x-ray. Clinical examination showed his lower liver margin to be about two inches below his rib margin. With this picture on August 9th and with the history of his illness from July 28th as it was, we believed it was unwise to treat him by operative measures at this time. We believed it best to delay until there was definite localization. In a few days the appendiceal symptoms cleared entirely. The only tender area that remained was around his gall bladder. In ten days' time his abdomen was quite lax on examination. The area of liver dullness still remained increased, at least 2" below rib level. The level of his diaphragm on his right side was at least 2" higher than on the left side, with some decrease in movement. His temperature remained slightly raised for the most part, although rarely going above 100 degrees or 100½ degrees. We believed he had a localizing area of pus some place, but were unable to definitely locate it. A subphrenic abscess was in our minds although it was difficult for us to understand the cause of it, as the disturbance around his liver region preceded his appendicitis.
>
> About the 25th of August he was seen by Dr. Y— a medical consultant. At this time he had a definite pleural friction rub on his right side. The area of liver dullness remained about the same. His abdomen was soft. Dr. Y— believed he had pus some place, probably in his subphrenic region, but he did not think we were justified in any exploration at that time and advised further delay. In the early part of September he began to run a more marked septic temperature. He was seen by Dr. S— at this time. Dr. S— could not say even at this time where the pus might be but believed it was probably around his gall bladder. On September 7th Dr. S— made a high right rectus exploratory incision. On breaking through some adhesions on the upper surface of the liver an abscess was opened into containing about a pint of pus. This abscess was between the liver and diaphragm but more to the lateral region. The abscess proved to be sterile, as there was no growth on culture. Drainage tubes were inserted. Mr. H— has gradually improved. His temperature has been normal for over a month. The tubes have been out more than two weeks. He still has a discharging sinus which leads upwards and outwards about 3", from which there is a moderate amount of drainage.——"

Mr. H— left the hospital on November 7. About two weeks later he had a severe diarrhea, without blood, having seven to ten movements in twenty-four hours, five to seven of which came during the night. After four days he became constipated, as he had been before. Except for this bowel upset he continued to do well, gaining in strength and weight, without symptoms or fever until December 3. On this day he had slight discomfort in the region of his sinus and an afternoon temperature of 101 degrees. There was little change in the character or amount of discharge which was blood tinged and sufficient to saturate four large dressings daily.

Examination was negative except for a high right rectus scar with a small sinus which was discharging a large amount of thick, glistening, mucopurulent material of a brick red color.

Discussion. The absence of any satisfactory cause for a subphrenic abscess pointed strongly to an abscess of the liver which had broken through into the subdiaphragmatic area as the probable source of the pus in this instance. For practical purposes the only "sterile" abscess of the liver which one sees is that due to the entamoeba histolytica. In fact, any liver abscess which fails to show a growth on ordinary culture media is to be considered as amoebic in origin, until proved otherwise.

With this in mind, it was learned that he had been in Chicago from June 20 to July 6, during which time he had stayed at one of the hotels involved in a number of amoebic infections.

He was taken at once to the Palmer Memorial Hospital where Dr. Shields Warren reported motile amoeba in both stool and discharge from the sinus.

His admission temperature was 98 degrees, pulse 80, respirations 20, white blood count 12,600, red blood count, 4,870,000, hemoglobin 75 per cent; differential: poly. 51%, lymph. 34%, large mono. 13%, eosinophiles 2%.

This case of amoebic abscess of the liver is reported before the final results of emetine therapy can be ascertained because:*

1) It represents a serious complication of an

*McKittrick — Surgeon, New England Deaconess Hospital. For record and address of author see "This Week's Issue," page 1298.

*NOTE: Under the direction of Dr. Albert A. Hornor this patient was given 8 grains of emetine hydrochloride in ten days. On the fourth day there was marked symptomatic improvement and a marked diminution in the amount of discharge. At the end of ten days he had gained six pounds. His discharge had almost entirely disappeared, although there were still a few amoeba present.

amoebic infection without a preceding history of diarrhea, a fact well recognized where these infections are common but not by those of us who see them but rarely.

2) It is particularly important at this time for the surgeon to recognize that a "sterile" abscess of the liver is of amoebic origin until proved otherwise.

3) The administration of emetine combined with aspiration rather than with external surgical drainage of the abscess is the treatment of choice, when there is no secondary infection[1, 2].

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TOXEMIAS OF PREGNANCY*

A Critical Review of the Recent Literature

BY DAVID HURWITZ, M.D.†

THE literature on the toxemias of pregnancy has been so extensive that occasional surveys and critical reviews are of aid. For this reason an attempt is made to summarize and discuss the recent literature on this subject. Toxemia of pregnancy is a common complication of pregnancy occurring about one in every twenty admissions to the Boston Lying-In Hospital. It occurs usually in the last trimester of pregnancy. Its diagnosis is based on hypertension (140 + mm. of mercury) or albuminuria, or both. Presenting symptoms are usually headache, visual disturbances (varying from slight blurring to amaurosis), epigastric pain or vomiting, edema of extremities and face. In severe cases, convulsions and coma may occur (eclampsia). It is frequently difficult, if not impossible, to differentiate acute toxemia and nephritis, or patients with antecedent hypertension during the active stage. This will be discussed more fully below. They are included under the general group of toxemias of pregnancy. From the above definition, vomiting of pregnancy is not included in the group (although some of its interesting features are discussed in this paper). "Acute yellow atrophy" included under many classifications is also omitted.

The lines of investigation have been quite diverse. The author will attempt to discuss them under the following heads:

1. Chemistry
2. Tests of Function of Organs
3. Circulatory Changes
4. Pathology
5. Clinical Aspects
6. Etiology and Pathogenesis.

1. Chemistry

Perhaps no aspect of toxemias of pregnancy has been studied more carefully than the chemical. So far as aiding in the clinical management of toxemia or in throwing light on the etiology of this condition, it has borne little fruit. Especially is this true in the routine chemical tests of the blood such as non-protein nitrogen, blood urea nitrogen, uric acid, etc., for these tests are of little aid in differentiating toxemias and chronic nephritis, or in prognosis.

Several studies have been of interest, among them the recent investigation of the acid base balance of normal pregnancy and the toxemias.

Acid base balance

In order to gain a true evaluation of the acid base changes in toxemia of pregnancy, we must first see what changes occur in normal pregnancy. There have been differences of opinion as to whether normal pregnancy is accompanied by acidosis or alkalosis. All investigators agree that there is a lowering of the plasma bicarbonate. This has also been found in dogs (MacNider[6]). Marrack and Boone[7] determined the PH of plasma colorimetrically by the method of Cullen. They found an increase of PH, decrease of CO_2 tension, and reduction of the plasma bicarbonate. They interpreted this as a result of hyperventilation, which lowers the CO_2 tension which in turn results in a fall of bicarbonate and an increase in PH. Gaebler and Rosene[2] also found increased PH and lowered plasma bicarbonate in normal pregnancy. They quoted Zuntz who observed three patients carefully during pregnancy, and found that two had increased respiration (60 per cent above normal). Oard and Peters[11] objected that the PH was not determined accurately because it was done colorimetrically. They made a total acid base equilibrium study of the serum in normal pregnancy, and found that there was a reduction of the total base and a concomitant and equal reduction of the anions. They believe the term "acidosis of pregnancy" is misleading because the reduction of alkaline reserve is due to the lowering of base rather than to the accumulation of acids. Further, they do not believe the low base is due to hyperventilation because the chlorides are normal (in hyperventilation, chlorides go up to compensate for the lowering of CO_2). Peters and Kydd[12] found the PH to be within normal ranges in normal pregnancy. Rossenbeck[14, 15] on the other hand, found increased chlorides in pregnancy. From these contradictory observations one can say only that pregnancy is accompanied by lowering of the total base and of CO_2 (bicarbonate), and that "acidosis of pregnancy" is a misnomer although it has not been settled whether the PH is normal or slightly elevated.

Kydd, Oard and Peters[3] conclude from their

*From the Department of Obstetrics, Harvard Medical School, and the Boston Lying-In Hospital.

†Hurwitz—Research Fellow in Obstetrics, Harvard Medical School. For record and address of author see "This Week's Issue," page 1298.

study of toxemia of pregnancy that "disturbances of the electrolyte and acid base equilibria in the serum appear to be referable to symptoms of the conditions rather than to the fundamental character of the toxemia". These disturbances are most marked in (1) convulsions, and (2) vomiting of pregnancy. Kydd, Oard and Peters[3] found changes in toxemia with convulsions to be similar to those in severe exercise. (These agree with the findings of Stander, Eastman, Harrison and Cadden[18].) Wirz[19] also found an increased [H+] in eclampsia as a result of seizures. He maintained that if it were not a result of seizures it would be present in pre-eclamptic blood, a condition which he did not find.

Rossenbeck[14,15] made a chemical analysis of organs removed at autopsy in normal pregnancy, nephropathy, and eclampsia. He calculated $\frac{\text{potassium}}{\text{calcium}}$ ratio and found that in normal pregnancy there is a shift toward the potassium while in eclampsia there is a shift toward the calcium. This agrees with the findings of Seitz and Spiegler who found that in pregnancy there is a rise in the galvanic nerve muscle irritability, while in eclampsia paradoxically there is a decrease of about one-half.

Kydd, Oard and Peters[3] studied five cases of vomiting in pregnancy. In none did they find free acid in the vomitus. The CO_2 content in the serum was decreased, the serum chloride was either normal or low, the PH normal, and serum protein high (indicating dehydration). We have examined vomitus from six patients with vomiting of pregnancy. Three showed free hydrochloric acid (7-23 degrees) in the vomitus. Of these three, two had blood analyses and these showed lowering of the serum chlorides and elevation of the CO_2. Those without free HCL gave normal or slightly lower values for CO_2 and normal values for the chlorides, findings which suggest that there is a correlation between the loss of hydrochloric acid and the tendency toward alkalosis. One must remember that gastric hydrochloric acid is decreased in pregnancy (Arzt) so that the loss of chloride by vomiting is also diminished.

From the above observations, it is apparent that (1) normal pregnancy is accompanied by a definite lowering of plasma bicarbonate. There is at the same time a lowering of the total base. Whether these changes are caused by a hyperventilation during normal pregnancy and are associated with an increased PH (alkalosis), (Muntwyler et al[8]), or are unaccompanied by hyperventilation or change in PH (Peters et al[12, 13]) awaits further observation. At present, the evidence leans toward the latter view. (2) The changes in acid base balance in toxemia appear to be the result of features of the toxemia (vomiting, convulsions) rather than the cause of it. Otherwise, they are the same as those of normal pregnancy.

Serum protein

During gestation and toxemia there is a decrease in the total protein, and slight relative increase in the globulin. Plass and Matthew[27] found that plasma protein begins to fall in the third lunar month, decreases gradually toward the sixth month, and then rises slowly to term. There is a slight rise during labor, and one day postpartum, followed by normal values. They also found that the serum globulin showed slight increase, and fibrin reaches the high point shortly after delivery.

Eastman determined the albumin-globulin ratio and obtained the following results:

Normal non-pregnant	1.7
Normal pregnant	1.6
Pre-eclamptic and eclamptic	1.3

With persistent albuminuria, serum protein may fall to 5 Gm.%, which is the edema level (Eastman[21]). Albumin is frequently lost in the urine during the puerperium of normal pregnancy (Eufinger[22, 23]). Eufinger believes that loss of albumin in the urine is a result of metabolic disturbance denaturing the albumin. He found the $\frac{\text{albumin}}{\text{globulin}}$ ratio at the end of pregnancy was 0.81, and in eclampsia 0.21. The latter figure seems incredibly low. Our figures are nearer Eastman's figures above. Kydd, Oard and Peters[20] found lower serum protein in edematous cases than in non-edematous cases.

Lash and Welker[25] studied the effect of serum protein by injecting albumin and pseudo globulin from eclamptics into mice in large doses. There was no toxic effect.

Calcium

During pregnancy there is a gradual diminution of total serum calcium (Cantarow[29]) corresponding somewhat to the change of plasma protein (Plass and Bogert[26]). Recently, Oberst and Plass[38] found a significant correlation between the serum protein and the serum calcium in non-pregnant and puerperal women, which is completely lost in late pregnancy and parturition when the protein range is considerably widened. The ratio of diffusible calcium (from the spinal fluid) to the non-diffusible calcium is increased in normal pregnancy through marked decrease of non-diffusible calcium. Bokelmann and Bock[28] state that the increase of ionized calcium in pregnancy facilitates calcium entry into the tissues and the storage of calcium in the placenta. In toxemia, the $\frac{\text{diffusible calcium}}{\text{non-diffusible calcium}}$ ratio decreases because of marked decrease in the diffusible calcium which suggests a diminished cell permeability. We do not believe these

findings definite enough for clinical interpretation. Feinberg and Lash[31] could find no appreciable relationship between blood calcium and eclampsia.

Of interest are the experiments of Minot and Cutler[35] in which carbon tetrachloride poisoning was produced in dogs. The dogs developed twitching, occasionally generalized convulsions, bloody diarrhea, and coffee ground vomiting. Following the symptoms of nervous irritability, depression and death would supervene. Bilirubinemia, retention of guanidine, and lowering of the blood sugar were found. They found that calcium relieves the hypoglycemia and symptoms, but glucose, while it raises the blood sugar, would not alleviate the nervous symptoms. They applied the results to a few eclamptics and believed that calcium is of therapeutic value. Symptoms were more severe when animals were on a meat diet. If calcium were added or a mixed diet were given, the animal developed a high tolerance to the poisoning. Against this, Rossenbeck[14, 15] found no lowering of the calcium in eclampsia, although it was present in normal pregnancy. These experimental conditions are remote from the situation in eclampsia and the results, although interesting, are not directly applicable to eclampsia.

Acetone bodies

During pregnancy there is a slight increase in acetone bodies which Stander and Cadden[42] believe might explain in part the lowering of the total base. Harding and Allin[41] found a normal renal threshold in pregnancy for acetone bodies and called attention to the raised metabolism in the latter half of pregnancy, and loss of anti-ketogenic substance through decreased urinary nitrogen as a factor in favoring increased acetone body formation. The acetone bodies in the blood of eclamptics triple their value in normal pregnancy (Stander and Cadden[42]). Bokelmann and Bock[40] noted even higher rises, but found no correlation between the level of acetone bodies and the severity of the case. They also noted the marked facility with which pregnant cases developed acidosis. A one day fast causes a six fold or higher rise in the acetone bodies.

Spinal fluid

Little recent work has been done on spinal fluid in toxemics and eclamptics. Schpoljansky and Danzig[43] found that the spinal fluid PH varied from 6.36 to 8.91. There was no correlation between the severity of the case and the PH. They state that disturbance of the PH causes the disturbance of the sodium, potassium and calcium which cause changes in the irritability and permeability of cells, and is the immediate cause of irritability of the motor cortex. This work does not appear to be well-founded.

Zweifel and Scheller[44] studied cerebrospinal lactic acid in eclampsia and found that it followed the blood lactic acid. It went up with the convulsions and, he believes, because of the convulsions.

Cholesterol

Cholesterol is elevated during pregnancy. Eufinger[45] found that in spite of the rise in total cholesterol, the free cholesterol is lower. He believes the cholesterol is denatured and excreted in albuminuria and eclampsia. It is interesting that he found doubly refractile bodies in the urine in two out of eight cases with marked albuminuria, and eighteen out of thirty-one with eclampsia. We have also occasionally found doubly refractile bodies in the urine of toxemic patients with slight albuminuria, and no inversion of the albumin-globulin ratio. These patients were mild toxemics who became entirely normal after delivery. Elevated blood cholesterol and doubly refractile bodies in the urine of pregnancy do not justify a diagnosis of nephrosis.

Carbohydrates

Titus and Willetts[60] found that eclamptic convulsions were preceded by sharp falls in the blood sugar. They determined plasma and corpuscular sugar, and found that when corpuscles were deprived of sugar, convulsions resulted. During recovery the plasma sugar goes up first, then the corpuscular sugar rises. They believe vomiting of pregnancy occurs in the morning because of starvation in the night and resulting low blood sugar. They recommend twenty-five per cent glucose intravenously. Thalhimer[50–54] after successful treatment of non-diabetic postoperative acidosis with glucose solution tried it on toxemias of pregnancy with good results. Stander and Harrison[49] did not find significant blood sugar fluctuations in eclampsia. We have not found consistent lowering of the blood sugar (Folin-Wu method) in our cases of eclampsia or vomiting of pregnancy and do not believe it has any causal relationship although intravenous glucose is of definite value in vomiting of pregnancy.

Dieckmann and Crossen[46] believe that there is a deranged metabolism of carbohydrates beginning with the steady loss of carbohydrates through storage in premenstrual endometrium which is continued in the decidua of pregnancy. There is also a loss to the fetus. These predispose to any vomiting of pregnancy. Intravenous glucose tends to remedy this defect.

2. Tests of Function of Organs

Liver function tests

Liver function tests have been studied repeatedly in the hope that they would reveal early changes in the liver. The difficulties are that the liver has so many functions that it is hard to get a correct idea of its functional state

from any single test. Siegel[94] using the bromsulphalein test believed it useful in differentiating neurotic and toxic vomiting, and perhaps useful as an aid in prognosis in eclamptic cases. E. L. King[87, 88] found that the phenoltetrachlorphthalein and bromsulphalein tests showed retention in cases with liver damage, and distinguished nephritic from toxic types, but did not believe that they furnished any aid in the prognosis which cannot be obtained from a careful clinical study. He also found that the van den Bergh test was positive in hyperemesis, and is of the non-obstructive type. Berman[83] found that the test had no practical value in the management of toxemias.

Experimentally Kamata[85] perfused a series of pregnant rabbits with $(NH4)_2\ CO_3$ to determine the urea formation power of the liver. He found accelerated liver functions at the end of the first and middle periods of pregnancy but a hindered urea formation at the end of the last period which disappeared on the first day postpartum.

G. King[89] found the levulose tolerance test abnormal only in pre-eclamptic toxemias and eclamptics, and Kaufmann[86] found by means of levulose tolerance, insulin effect on blood sugar, and bilirubin test that derangements of liver functions occur in normal pregnancy; Stroebe[96] found these changes more marked in pre-eclamptics and eclamptics.

MacKenzie[91] found that urobilinuria is not usually present to a pathological degree in nephritic toxemia but is generally found in hepatic types. We do not believe that such a clinical distinction is possible or that any liver function test would reveal it.

In general, liver function tests are of no value in diagnosis and prognosis in toxemias. Kaufmann's combined tests of liver function show that derangements may occur in normal pregnancy.

Renal function tests

For some time investigators have tried various tests of renal function in an effort to separate toxemia from chronic nephritis, and to follow the renal function after toxemia. The current methods such as the phenolsulphonephthalein, two hour renal, and Mosenthal tests have not been of value. Stander, Ashton, and Cadden[101] in a comparative study of the Mosenthal, phenolsulphonephthalein, diastase, urea concentration factor, phosphate, urea clearance, guanidine, and creatinine excretion, found that the last three were of most value in this work. Krieger[99] found the urea concentration test more discriminating. Recently Hurwitz and Ohler[97] made a comparative study of blood chemistry, phenolsulphonephthalein, and one-hour renal test for dilution and concentration, and urea clearance in groups of normal pregnancy, toxemia, eclampsia, and chronic nephritis. The tests other than the urea clearance did not aid in differential diagnoses, while urea clearance gave normal results in normal pregnancy and toxemias, and low results in chronic nephritis and eclampsia (with rapid return to normal after delivery). They believe the urea clearance is a valuable renal function test, especially in following the renal functions of individual patients over a period of time, where it is probably of more value than in diagnosis and prognosis during the acute stage. Especially is this true because the dilution—concentration tests, usually considered a good clinical test outside of pregnancy, give abnormal values in normal pregnancy (Janney and Walker[98]).

3. Circulatory Changes

Capillary changes have been emphasized by the German investigators particularly Hinselmann[104, 105] and Nevermann[112] who find in edema of pregnancy, mild toxemia, pre-eclampsia and eclampsia, capillary changes similar in type, but different in intensity. The capillaries at the base of the nail show lengthening but no tortuosity of the loops. There is thickening of the venous loop, stasis, and granular flow. There is also vascular spasm. Occasionally the arterial loop suddenly disappears and then the venous loop disappears as though a peristaltic wave had passed over them. Similar changes were noted in the peritoneum and uterus and other organs at operation. After venesection, the tempo of the flow is changed, stasis is decreased, and vascular spasm is less marked. Mufson[110] studied capillaries in a series of cases in hypertensive toxemia but did not find any consistently typical picture. He found that the toxemias with low capillary blood pressure gave the most favorable maternal and fetal result while those with high capillary blood pressure carried a poorer prognosis. He also found that capillary pressure was reduced by magnesium sulphate.

Some studies have been made of blood vessel changes in the eye. Cheney[102] found that changes in the fundus were most common in the last three months of pregnancy. He quoted Schiotz who says that if a toxemic patient has retinitis, the chances are four to one that she has nephritis. Mylius[111] in a careful study of eye grounds in eclampsia and pre-eclampsia by means of the Nordenson camera demonstrated the occurrence of spastic and tetanic vascular process in eight out of twelve cases. The picture is surprisingly manifold. In mild forms trough-like indentations run over the vessel branches. This is followed by a quiescent period after which the peristaltic-like waves begin. Especially in the early state, the process may be marked for a short time and then be lacking for a variable time. This process changes the external form of the vessels making them predominately spindle or rosary shape without changing the course of the vessel. This peristaltic process may progress to a stationary or tetanic form giving a

picture of narrow vessels with streaks. Thus the diagnosis of severe retinal change can be made falsely if one does not know the early condition of the retinal vessels. All of these changes gradually but completely regress after completion or interruption of the pregnancy, thus demonstrating their purely functional character. The onset of retinal plaques and edema (frequently found in toxemia by Pillat) is preceded by marked engorgement of the veins. Mylius[111] believes that the changes in the retina are not due to anemia as Volhard believes, but to the slowing of the blood stream and accompanying hyperemia in the part distal to the spasm. These changes are similar to the changes in the glomerular capillaries in malignant nephrosclerosis found by Shapiro[113] who observed in the distal portion of the glomerulus a slow granular flow similar to that obtained by Hinselmann[104, 105] and Nevermann[112] in the finger of eclamptics.

These studies are based on a method which has a large subjective factor. This is minimized in Mylius's study with the Nordenson camera. The results are in keeping with the hypertension and the pallor of toxemics, and are in keeping with the concept of toxemia as a vascular disease, but final acceptance awaits a more objective method.

4. Pathology

The typical lesion in the liver of eclampsia is considered to be a necrosis in the periphery of the lobule and portal spaces, in which blood cells may or may not be present (Williams[128]). Schmorl attributed these changes to thrombotic processes in the smaller portal vessels. Recently Davidson has found these three different types of hepatic lesions in eclampsia:

1. Necrosis of the cells of the peripheral zones of the lobules.
2. Widespread necrosis of the cells in the central and mid zones.
3. Small areas of focal necrosis with no gross lesion. These findings were also observed in severe toxemias without convulsions. Acosta-Sison[115] found focal areas of hemorrhagic necrosis and fatty degeneration predominating in the periphery of the lobule, and liver lesions scattered throughout the lobule with special susceptibility of the central areas. She also found severe organic lesions similar to the eclamptic in toxemia without convulsions. From the above one may say that mid zonal and central lesions occur with great frequency, and that peripheral lesions are not the sine qua non of eclampsia.

The kidneys are rarely unaffected. Bell[117] states that no such report should be accepted unless a careful macroscopic and microscopic examination be made. Fahr found in the kidney of eclamptics the following changes:

1. Swelling of the glomerular loops.
2. Albuminous degeneration of the convoluted tubules.
3. Hemoglobin cylinders in the tubules.
4. Degenerative changes in the arterioles—arteriolitis.
5. Thrombi in the glomerular loops.

He found a widening and swelling of the glomerular capillary wall, and the loops may appear bloodless. Hyaline changes and occasional fat deposits are found in the loops. The tubules show marked albuminous degeneration which may advance to hyaline degeneration and fatty changes. The smaller arteries, especially the afferent arterioles, are frequently involved. Fahr states that the glomerular changes are due to arteriolar spasm.

Bell[116] found that the narrowing of the glomerular vessels was due almost entirely to a massive thickening of the capillary basement membranes which is fairly characteristic and may be differentiated from the changes in nephritis and hypertension. He states that "the clinical evidence indicates that the eclamptic kidney usually heals rapidly, but in some instances very slowly. There is a possibility of passing into a definite chronic nephritis with contracted kidneys, but there is no convincing evidence that this occurs." The essential nature of the disease Bell believes is an injury of the glomerular capillaries which allows albumin to escape and impedes the flow of the fluid through the kidneys. The glomerular lesion may be the primary cause of the hypertension he believes. In one case of hyperemesis gravidarum Bell found glomerular lesions which correspond entirely to those of typical eclampsia.

Brain

Braunmühl[120] examined three brains from eclamptics and found severe degenerative processes belonging to the group of ischemic cell disease, and believes the eclamptic seizure is ushered in with a vasoconstriction. Jaffé[124] says that the primary occurrence is a vascular spasm which leads to angionecrosis, and that after the spasm is released, the inshooting blood causes vascular rupture. Benoit[118] and de Vries[122] also attribute the patchy character of the changes to a primary spasm of the cerebral arteries and arterioles. These changes are interesting in the light of Spielmeyer's findings of functional vascular spasms or some influence on the vascular nerves which play a basic rôle in the seizures of epilepsy.

In sudden death in toxemias without convulsions Pohl[126] emphasized the frequency of hemorrhage into the third and fourth ventricles as a cause.

5. Clinical Aspects

Classification

Various attempts have been made to classify the toxemias, but it must be remembered that there is no sharp dividing line between the various types. Seitz calls the entire group Oednek-

lose (oedemo-nephrotische-eklamptische) believing that the three types are part of the same process which may vary in severity in different individuals. Stander and Peckham[133] classify the toxemias of the latter half of pregnancy as follows:

1. Eclampsia.
2. Pre-eclampsia (similar to No. 1 except for the absence of coma or convulsions).
3. Chronic nephritis.
4. Eclampsia superimposed upon nephritis.
5. Low reserve kidney.

The two groups about which there is the most difficulty are the chronic nephritic and low reserve kidney groups. The authors include in the chronic nephritic group those patients who show a rise in blood pressure and albumin early in pregnancy, usually with more difficulty in the present pregnancy than in the previous ones. Absence of albuminuria, edema, symptoms and signs of decreased kidney function in the presence of hypertension does not speak against underlying nephritis. According to the authors "essential hypertension" is a dangerous term. On the other hand we believe there is a definite group of patients who have hypertension before or during the first few weeks of pregnancy without signs or symptoms of nephritis. Such cases have been reported by Williamson[134]. Primary arterial hypertension is common enough so that its complication by pregnancy need not be considered a rarity. Further, there are cases that develop moderate hypertension during the pregnancy, continue with a hypertension of even 180 to 190 systolic after they are delivered, and cannot be diagnosed as nephritics on the bases of renal studies even though they or the fetus run into trouble in the present or subsequent pregnancies. All we can say is that they have vascular hypertension. To say that they have nephritis because they may go on to renal deaths is not rational, for subsequent cerebral or cardiac deaths are probably more common in this group. It is very possible that one of the reasons for the increased incidence of hypertension in the female is the factor of pregnancy with its frequent occurrence of vascular disturbance.

"The low reserve kidney" group apparently is differentiated from the pre-eclamptic group mainly by the blood pressure which should not be above 150 systolic in the low reserve group. However, fatal eclamptic cases have been reported with blood pressure no higher than this, and eclamptic lesions noted at autopsy. Further there is no evidence of renal damage other than the albuminuria (which may be very slight and which is present in the pre-eclamptic group as well).

Corwin and Herrick[129] give the following classifications:

1. Acute convulsions or eclamptic toxemia.
2. Nephritic toxemia.
3. Hypertension, or cardiovascular toxemia.

The essential hypertension occurring before pregnancy exhibited the latter type of toxemia almost without fail. "Child bearing can reveal essential hypertension when it is latent, and aggravate it when it is active." These authors stress the effect on the cardiovascular system. Later, Herrick[130] classified toxemias into (1) nephritis and (2) pre-eclamptics and eclamptics. "The latter group has an important hypertensive vascular basis and is related to hyperpiesia." The nephritic group included all non-convulsive cases with a non-protein nitrogen above 40 mgs. per cent and all those with marked and long-standing albuminuria. On the whole, this classification probably forms the best working basis. The diagnosis of chronic nephritis of pregnancy can rarely be made safely during the acute stage (just before delivery).

It has seemed to us that the vascular element in toxemics is more important than the renal. A sudden hypertension with vasoconstriction may give the eclamptics pallor, convulsions (through anemia of brain) and albuminuria. The vascular effect may be apparent after delivery when it is found that the patient has a significant hypertension (frequently called nephritis on this basis).

Sequelae

The sequelae of toxemias of pregnancy are not so benign as was formerly believed. Corwin and Herrick[129] found that more than one-third of the eclamptics showed signs of serious vascular disease six weeks to six years postpartum. Peckham[140] found in a follow-up study of seventy-seven cases of eclamptics that 22 per cent had "definite though mild chronic nephritis a year or more after the attack" (probably some of his cases are hypertensive). Peckham and Stout[141] found that in a large follow-up series of toxemic patients, 40 per cent have been found to have definite chronic nephritis. Donovan[136], Harris[138], Kellogg[131], Young[146], and others have obtained similar results. Many of these patients are classified as nephritics although the evidence consists only of an elevated blood pressure. We may say that toxemic patients are prone to develop vascular hypertension subsequently which may run the course of hypertension outside of pregnancy.

6. Etiology and Pathogenesis

The toxin in toxemia has been the object of prolonged search. The pathology has been reproduced by injections of tissue fibrinogen. (Dieckmann[153] and Wooldridge, 1899 quoted by Theobald[171].) Bodenstab[151] found an increase of vasoconstrictor substance in blood of toxemias.

The most important contribution is that of

Anselmino and Hoffman[148, 149, 150]. These investigators used a method for determining pituitrin in the blood based on its anti-diuretic and blood pressure raising effect in rabbits. An ultra-filtrate from blood of toxemics was prepared by filtering the plasma through a collodion membrane. The ultra-filtrate was injected subcutaneously into rabbits after passing a sound into the stomach and injecting 90 cc. of water. The blood pressure effect was observed by exposing the carotid artery and observing the manometric pressure at which it could be occluded. They found the anti-diuretic substance in all cases with "nephropathy" and eclampsia with clinical edema which disappeared within twenty to thirty hours with one exception (a puerperal eclampsia). In the blood of healthy pregnant patients and in pregnant patients with hydrops it cannot be demonstrated with certainty. They found a relationship between the content in the blood of anti-diuretic substance and the severity of the clinical picture. In all cases with elevated blood pressure (180 mm. +) they found the blood pressure elevating substance. The anti-diuretic and the blood pressure elevating substance can occur in blood independently. The pituitrin theory of toxemias gains support from many sources:

(1.) Trendelenburg and Rowntree obtained coma and convulsion in animal after forcing water. Recently, the importance of water retention has been emphasized in epilepsy (McQuarrie[166, 167, 168]) and Arnold and Fay[181] have extended it to eclampsia and pre-eclampsia. Peripheral and pulmonary edema are common in eclampsia.

(2.) Voegtlin and Dyer produced hemoglobinuria in animals after injecting pituitrin.

(3.) Seitz, and Spiegler and Schol found lowering of the galvanic nerve muscle irritability, while Eddy and Yoskrinito obtained the same results after pituitrin administered to hogs.

(4.) Capillary spasm, coma in eclampsia (see above). Pituitrin causes narrowing of the capillaries, and paling of the skin after the injection.

(5.) Molitor and Pick found that certain drugs weakened the effect of pituitrin. The same drugs have been found especially to be of value in the treatment of toxemias.

Furthermore, by various chemical tests this substance has been found to behave similar to pituitrin. Fauvet produced a pathology similar to that of eclampsia by the repeated injection of pituitrin.

This fits in with the current concept of toxemias as being due to a vasoconstriction. (See circulatory changes, above.)

Arnold and Fay[181] have recently described a method of fluid balance and dehydration in the pre-eclamptic, dangerously threatening and actively convulsive groups, and the moderately pre-eclamptic group, the total fluid intake is regulated so as not to exceed the urine output of the first twenty-four hours (usually 600 cc.). Small daily doses of magnesium sulphate are given. Diet of solid foods of wide varieties including protein is given. The patient is fed well but moderately; a salt-low diet, soft and liquid nourishment high in water content being avoided, as are also sweets and desserts. In the dangerously threatening pre-eclamptics, the above treatment plus intravenous glucose 50 cc., 50 per cent every four hours if necessary for dehydration, and spinal drainage in 15-30 hours if no improvement. In the eclamptic group, two to three grs. sodium luminal is given and repeated every two hours if necessary. Morphine is given only after glucose and spinal fluid drainage has been done. Although the series is small, the data are very suggestive. We have steadily maintained that there is no rationale in forcing saline intravenously and subcutaneously into patients with anuria or oliguria with the idea of washing out the kidneys. The fluids (often six liters or more per twenty-four hours) are retained to a large degree exaggerating edema. Edema is a common finding in post-mortems of eclamptics and is especially marked in the brain and lungs.

The use of intravenous glucose (without saline) to combat the oliguria or anuria of severe pre-eclampsia and eclampsia is widespread and its results are reported to be quite favorable. Glucose is metabolized or stored leaving the water to be excreted if there is no extra salt to keep it back*.

The retention of water fits in well with the Anselmino and Hoffman pituitary theory.

There are certain therapeutic implications from the above data:

1. Morphine is a good drug for eclampsia (inhibits the effect of pituitrin).
2. Pituitrin is better omitted from the clinical management of toxemias. Pitocin is equally effective in inducing labor and has very slight anti-diuretic effect.
3. Salt and fluids should be restricted during the toxemic period, especially when edema is present.

Further, there is no evidence that a moderate protein intake is of any harmful effect in the course of toxemia. In fact, it has been shown to be harmless in nephritis (Keutmann & McCann[194]). Anemia develops quite easily in pregnancy and the dietary is important (many

*Recently Newburgh and Lashmet (Am. J. Med. Sc. 186:461 [Oct.] 1933) have emphasized the importance of treating water quantitatively in the handling of patients with nephritis. Since diseased kidneys are unable to put out a concentrated urine, withholding fluids would tend to prevent the excretion of all the solids. They forced fluids, their patients improved, edema decreased, and the NPN went down. Of course salt was withheld.

Along similar lines it would be best to withhold saline in patients with eclampsia and give intravenous glucose. The glucose is metabolized or stored leaving water free to act as a diuretic. If patients can drink, forcing fluids with a salt poor diet might be effective.

women become achlorhydric during pregnancy). Recently, we saw a woman who had been on a meat-free diet for eleven years after a toxemic pregnancy and presented herself in another toxemic pregnancy with a marked secondary anemia.

Conclusions

From a comprehensive review of the literature on toxemias of pregnancy, one may make the following conclusions:

1. Blood chemistry is of little value in the clinical management of toxemics.

In normal pregnancy, there is a lowering of plasma bicarbonate and of total base. Whether this is associated with an acidosis or alkalosis has not yet been definitely settled. Changes in blood chemistry in toxemia are the result of convulsions or of vomiting.

Lowering of the blood sugar in eclampsia and vomiting of pregnancy has not been confirmed.

2. Liver function tests are of no value in diagnosis and prognosis. There is possibly a slight derangement of liver function in normal pregnancy.

The urea clearance test is probably the most valuable renal function test in studying toxemic patients especially in following them over a period of time.

3. Changes in the capillaries at the base of the nail and in the retinal vessels have been noted by German investigators. On the other hand Mufson did not find any consistently typical picture of the nail capillaries. Final acceptance of capillary changes awaits study by an objective method.

4. The pathology of the liver is typically peripheral necrosis with or without hemorrhage. However, other types of liver damage are frequently found in eclampsia while pre-eclamptics may show liver lesions of eclampsia.

The renal lesion is important. It is probably vascular in origin (Fahr). Bell has described changes in the basement membrane which are fairly typical in eclampsia.

5. The classification of Corwin and Herrick[129] is probably the best at the present time. There has been a careless use of the term "nephritis of pregnancy" by obstetricians. One must remember that hypertension is a common disease and may occur in women of the child-bearing age.

6. The recent report of a pressor substance isolated from the blood of eclamptics and pre-eclamptics by Anselmino and Hoffman[150] is of the greatest interest.

7. There is need of a great deal of checking of basic facts in this field, among them, the question of alkalosis in normal pregnancy, capillary changes in toxemia, Bell's basement membrane changes in eclampsia, Anselmino and Hoffman's findings of pituitrin-like substance in the blood of toxemics, etc.

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CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 19511

PRESENTATION OF CASE

DR. AUGUSTUS S. ROSE:* A fifty-seven year old American salesman entered complaining of weakness and dark colored stools of four days' duration.

Four days before admission when the patient started to the bathroom he suddenly felt very weak and dizzy and everything seemed to go around. He sat down and broke out into a cold sweat but did not faint. He passed a small amount of inky black, well formed feces. There was no nausea or vomiting. He felt so weak that he was forced to go to bed, where he remained for the next four days. He continued to feel very weak and developed palpitation. His stools continued to be black.

He had never had abdominal pain. His appetite had always been very good. Rarely after eating a big meal he had sour belching, but this occurred only about once a week and was never accompanied by vomiting. Very rarely he had a small amount of pain with the belching, but this usually lasted for only a few minutes. His bowels had always been somewhat constipated, requiring a cathartic about twice a week. There was never any blood in his stools, which were always brown. He never vomited blood or dark colored material. He had never been jaundiced. His best weight was 145 pounds, several years ago. His present weight was 123 pounds. Five years before entry while in bed one night he suddenly felt dizzy. Since that time he had slept on two pillows; if he tried to sleep with his head lower than this he felt dizzy. The rest of the past history is irrelevant.

Four siblings were living and well. He had been married twenty-two years. His wife was living and well. She had had one stillbirth, following which she was sterilized.

He slept about nine hours each day. He drank two cups of coffee and one cup of tea and smoked three or four cigars daily. He had been unemployed for the past two years except for small odd jobs. He appeared to be very nervous but was apparently an intelligent man.

Physical examination showed a well developed and poorly nourished man showing moderate pallor of the skin and lips. He appeared to be very apprehensive and continually moved around. The teeth were very carious. The lungs were clear. The heart was normal except for very distant sounds. The blood pressure was 170/80. Examination of the abdomen was not very satisfactory. There was a fine tremor of his hands. Rectal examination was negative.

The temperature was 99°, the pulse 93. The respirations were 20.

On laboratory examination the urine was clear and showed a specific gravity of 1.015. There was no albumin, sugar or bile present. The sediment showed an occasional white blood cell. Examination of the blood showed a red cell count of 2,500,000 with a hemoglobin of 60 per cent Tallqvist. The white cell count was 9,200, 84 per cent polymorphonuclears. The smear was not remarkable. The stools were formed, black, and showed a four plus guaiac. The Hinton was negative. The non-protein nitrogen was 33 milligrams. A lumbar puncture was negative.

Four days after admission his red blood cell count was 2,400,000, the oxygen capacity 9.85 volumes per cent, the cell volume 25.80 per cent, the volume index 1.25 and the color index 1.10. He was put on a milk and cream diet and given liver extract. Following this treatment the red cell count rose to 3,700,000, with 6 per cent reticulocytes. The volume index of the cells was 1.04. A gastro-intestinal series two days later showed no variation from normal in the esophagus and stomach. The duodenal cap was grossly deformed. The loop appeared normal. On the following day a note was made that he had been free from occult blood in his stools for over a week. A surgical consultant advised operation.

X-RAY INTERPRETATION

DR. JAMES R. LINGLEY: There is nothing very remarkable in the x-ray films except that the deformed duodenal cap is typical of ulcer.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: Again I have to say that on first glance this looks like a perfectly clean cut situation. We have a man of fifty-seven who has sudden severe gastro-intestinal hemorrhage, who does not vomit blood and in whom we find later a grossly deformed duodenum by x-ray. If I saw the patient and were able to talk with him and to feel him I might be willing to disagree with the X-ray Department, but I should probably be wrong if I did. Therefore I accept the diagnosis of duodenal ulcer in this case.

Those of us who attended Dr. Perry Pepper's clinic the other day perhaps have an eye out for what he called the *x* factor, or the unknown factor in any given case. It seems to me that there is one definitely unknown finding here and that is that he was bleeding for four days, apparently a massive hemorrhage, with tarry

*Senior interne on the East Medical service.

stools, and by the end of those four days the blood pressure was 170/80. I think it is fair to say that patients with duodenal ulcer almost never have hypertension. I looked up one hundred cases once and I could find no case with a blood pressure over 150. It was very striking that most of the blood pressures were down, many as low as 110 and 120, even in older people.

DR. ROSE: I might say that the blood pressure later was 110, and stayed so until he was transferred.

DR. RICHARDSON: That makes a little difference. Still I think it is surprising that even two readings of 170/80 are to be found in a patient with peptic ulcer which has bled for four days.

In looking a little more critically then at the blood one is struck by another factor which is not quite explained, that is a volume index of 1.25. It is definitely higher than normal and is the type of thing we are likely to see in pernicious anemia. The color index was also a little higher than one might expect in hemorrhage alone, as was the cell volume. All of these figures I should think ought to be a little lower than normal rather than definitely higher than normal.

I wonder why they gave him liver extract, whether it was because he had a high volume index and they thought he had pernicious anemia. I think it is fair to say that pernicious anemia and active duodenal ulcer do not occur together. Dr. Murphy believes that in anemia due to hemorrhage, injection of liver extract intramuscularly along with iron in large doses hastens the recovery of the blood. Most people feel that iron in large doses is sufficient.

Taking these two things together, one wonders whether there may have been some primary blood disturbance that might result in ulcer with bleeding. There are only two such conditions which happen to occur to me. One is chlorosis, which this patient obviously does not have, and the other is polycythemia vera. Has this patient polycythemia?

If we go back over the story we have a history which has not been considered very much and that is that five years before entry while in bed he suddenly felt dizzy. One might interpret that as hemorrhage, but after that time he had to sleep on two pillows. If he slept with his head flat he became dizzy. Did that mean he had a red count of eight million and that when his head was down he had cerebral symptoms?

In regard to the question of operation, I certainly would agree that a man with a massive hemorrhage like this ought to have operation done. If one could say that he had a definite polycythemia would that influence one's decision? I think the ulcer requires a radical operation, because whether or not he has polycythemia he can perfectly well bleed to death.

I will make, then, a flat-footed diagnosis of a large ulcer in the posterior wall of the duodenum, and I will also say that this patient had polycythemia vera.

FURTHER HISTORY

DR. ROSE: Three weeks after entry under ether anesthesia a gastric resection with a posterior Polya anastomosis was performed. The ulcer seemed thickened on the superior margin of the duodenum. The fact that all this region of the duodenum was adherent to the pancreas however, indicated that the lesion extended posteriorly as well. The duodenal stump was easily turned in and a transmesocolic Polya anastomosis was done at the proximal end at the lesser curvature.

His convalescence was uneventful and he was discharged.

He was seen three weeks later in the Follow-up Clinic, where he reported no symptoms.

CLINICAL DISCUSSION

DR. TRACY B. MALLORY: We have taken up from time to time several of these cases of large chronic ulcers of the posterior wall of the duodenum with bleeding. Several of them the surgeons have attempted to operate on and the cases that come in the postmortem series have of course been the ones with unfortunate results. So I thought today I would give Dr. Allen a chance to tell us about one case that was cured.

DR. ARTHUR W. ALLEN: Looking up all the cases of massive hemorrhage which we have had in this hospital for twenty years, Dr. Benedict and I found some very interesting facts. We never knew whether a patient who came into the Emergency Ward bleeding from a duodenal ulcer would bleed to death or survive. We had no facts to guide us in the matter. The consequences were that these patients were all watched until they were well, or if bleeding continued, until they were obviously moribund before they were turned over to the Surgical Department. As a matter of fact no case of massive hemorrhage from duodenal ulcer survived operative procedure when done as a last resort. Eight attempts were made and twelve patients died from hemorrhage without operation within this period of time. About once a year, then, we should be prepared to decide early during a massive hemorrhage whether a fatal result is likely and subject the patient to radical surgery before he is entirely depleted.

Resection of the distal third of the stomach and the first portion of the duodenum in a quiescent stage is a very safe procedure and carries a very low mortality. So one point that we have learned from this study is that patients falling into a certain group should be advised strongly to have a radical operation as soon as they have recuperated from the acute episode. The

patient under discussion today was one who received and accepted this advice.

Other facts that came to light were as follows. Three per cent of all bleeding ulcer cases in this hospital die from hemorrhage. Fourteen and a half per cent of all cases that bleed massively and suddenly from duodenal ulcer die from hemorrhage. Only two patients out of twenty under fifty years of age were in the fatal group. That may sound complicated, but it means this, that few patients under fifty should be expected to continue to bleed, and it may be said that any man over fifty must be expected to bleed to death and must be watched with that in view.

If this man—I saw him shortly after he entered—had continued to bleed after he came into the hospital and had bled after a transfusion we would have immediately operated upon him before he became depleted, and I think that by a special technic which has been described by us in the October 1933 number of Annals of Surgery we can save some of these patients even when operation is necessary during acute hemorrhage. Looking back over the cases that were attempted in the past, I think most of the eight cases that did not survive would have done so had they been operated on when they first came in or within the first twenty-four hours, and operated on so that the hemorrhage did not continue during the operation.

Patients with sudden massive hemorrhage all have an eroded large vessel, which is usually a branch of the gastroduodenal or the pancreaticoduodenal artery. These vessels anastomose in such a way that three large vessels must be ligated in order to stop the hemorrhage. They all lie behind the duodenum. That means that the stomach must be lifted up and the ulcer operated on from behind.

Since we began this study we have operated upon about twenty of these cases in the quiescent stage without mortality, protecting them from further bleeding and we hope from further ulcer symptoms. If the operation must be carried out in the acute stage of bleeding, the mortality will of course be higher; but we believe if it is done early, i.e., as soon as it can be determined that bleeding is continuing, some will survive. No case however should be operated upon in the acute stage of hemorrhage unless there is evidence that spontaneous recovery is unlikely.

Diagnosis

Penetrating ulcer of the posterior wall of the duodenum.

Pathologic Discussion

Dr. Mallory: This man had a very adherent ulcer a portion of the posterior wall of which Dr. Allen left behind at the time of operation I take it, since we did not find anything but the edge of it in the specimen. We found also an acute erosion that had just healed over, and a very extensive gastritis.

Here is the duodenal mucosa, which you see in rather large shaggy folds. As we move along we come to an area where it is greatly thinned, and then on the other side we again get big shaggy folds, but here in between is an area where the superficial glands are entirely missing and there is only a single layer of cuboidal epithelium covering the whole area. There is no question that this spot was very recently eroded and has just healed within a few days.

This of course was a very minor part of the picture, but the more or less unknown factor, perhaps hyperacidity, which starts up periods of activity in ulcers probably activated the large old duodenal lesion and at the same time produced this very minute lesion which might very well have gone on to the formation of another serious ulcer if he had had many more successive attacks.

Since this patient also left the hospital perfectly well, we are not yet in a position to check Dr. Richardson's second diagnosis. A blood count perhaps six months from now would do it.

Dr. Allen: The reason there is no bottom to the ulcers in these specimens that have come to Dr. Mallory is that the floor of the ulcer is the pancreas. The entire wall of the duodenum is eroded. If it were not entirely eroded of course there would be no massive hemorrhage. In removing them surgically we have to leave what is the present base, which is pancreatic tissue.

Dr. Mallory: Dr. Bradley, have you any thought as to whether the gastritis may have been sufficient to account for the blood picture, which is slightly suggestive of pernicious anemia?

Dr. John I. Bradley: I do not believe I can contribute anything on that.

Dr. Mallory: A severe gastritis that has gone on to the stage of atrophy is often found in pernicious anemia, but I should hardly expect it at this period of the disease.

Dr. Richardson: Did he have a gastric analysis?

Dr. Rose: There was free acid before and after operation.

CASE 19512

Presentation of Case

Dr. Augustus S. Rose:* *First admission.* A Canadian housewife twenty-four years of age first entered the hospital ten years before her final admission with a complaint of epigastric pain, faintness and tarry stools.

These symptoms began with an attack three years before admission. One year and again three months before admission similar attacks

*Senior interne on the East Medical service.

had occurred. All three were characterized by pain of dull grinding nature starting in the epigastrium and radiating around her body in both directions, as well as through to the region of the right scapula. It usually occurred one and a half to two hours after her noon meal and did not cease until she went to sleep at night. Food did not give relief, but soda produced instant improvement. With the first attack she vomited a considerable quantity of blood and noticed weakness and pallor for three weeks following this. The second attack was characterized by a series of tarry stools, the last attack by further tarry stools, faintness, dizziness and ringing in the ears. Since the onset of this last attack the pain had not recurred but the faintness and dizziness were worse than on previous occasions.

The family history is non-contributory.

She had been married three and a half years. One child was living and well. There were no other pregnancies.

She had had the usual childhood diseases, including scarlet fever and repeated attacks of tonsillitis. During one of these attacks her joints had been painful and a physician had insisted that she stay in bed for some time because of "trouble with her heart". Her catamenia had begun at sixteen and had always been regular. There had been slight leukorrhea.

Physical examination at the time of entry was entirely negative except for pallor of the skin and mucous membranes and tenderness in the left lower quadrant of the abdomen. The heart was normal in size. There were no murmurs. The blood pressure was 120/68.

X-ray findings showed some questionable apical abscesses about her teeth. A gastro-intestinal series showed the stomach low and atonic. It emptied in normal time and appeared regular in outline. The first portion of the duodenum was large and active; a very small irregularity was consistently seen in its outline. This appearance was found at two examinations on successive days. The findings were considered suggestive of a small ulcer in the first portion of the duodenum.

Laboratory examinations showed a normal urine, a hemoglobin of 50 to 60 per cent, red cell count 3,600,000 to 4,880,000, white cell count 11,000. The blood smear was normal except for moderate achromia. Ten stools were guaiac-negative. A blood Wassermann was negative. Gastric analysis showed free hydrochloric acid 25, total acid 34 in the fasting contents; after the test meal free acid 35, total acid 55. Guaiacs were negative.

She was given a transfusion of 500 cubic centimeters of blood and placed upon a five meal gastric diet with bicarbonate of soda p.r.n. for gastric discomfort. She had one fairly severe attack of pain while in the hospital. She was seen by a consulting surgeon who advised operation on the basis of the repeated hemorrhages. The patient however elected to continue with medical treatment.

Second, third, fourth and fifth admissions. Four, three and two years before her final admission she was readmitted to the hospital, in each instance with a recurrence of certain of her earlier symptoms, particularly fainting spells and repeated tarry stools. Throughout this period she had had rather diffuse menorrhagia, and the fourth admission was for this symptom only. A dilatation and curettage was done and the cervix cauterized. The curettings showed no histologic abnormality. There was definite improvement in the metrorrhagia following this operation. During this ten year period there were intervals as long as two years in duration of absolute freedom from symptoms during which she usually broke her five meal diet régime and reverted to an ordinary three meal diet. On the other hand the recurrence of symptoms usually coincided with periods of domestic stress and strain, such as an attack of pneumonia in her daughter, the insistence of her husband's family that they live with them, and on the final occasion the information that her husband was suffering from an incurable disease.

A gastro-intestinal series was repeated on only one occasion, at the second admission, with completely negative findings in the stomach and duodenum.

At the fifth and last admission she was brought to the Emergency Ward again after an attack of fainting and the passing of several large tarry stools.

The physical examination was essentially unchanged from the previous entrance. There was again pallor of the skin and mucous membranes. The heart was not enlarged and there were no murmurs. The blood pressure was 130/80, the pulse 110, of good quality. There was slight tenderness in the left upper quadrant. The hemoglobin on this occasion was 55 to 60 per cent, the red cell count 3,350,000 to 3,910,000, the urine normal. The first stool was guaiac-positive, all succeeding ones guaiac-negative. The basal metabolism was —6. Gastric analysis showed no free hydrochloric acid, total acid 6.

X-ray examination on this occasion showed an eccentric duodenal cap with marked spasm and hyperactivity. It was flattened and irregular on its superior surface. The loop appeared normal. There was no six hour retention. A chest film was negative.

Clinical Discussion

Dr. Arthur W. Allen: In the first place this brings up a point that I should have men-

tioned in the other case, namely, that women are apparently very much less likely than men to have fatal bleeding from duodenal ulcer.

The reason for operation here was the persistence of symptoms. It has been brought out by Jordan and Keefer that patients with recurrence of symptoms in spite of diet et cetera are those who bleed. That is, bleeding ulcers are less responsive to medical treatment than those that do not bleed.

I presume we advised surgery in this case because she was having a persistence of symptoms and frequent recurrence of bleeding.

Apparently we resected a part of her stomach and the first portion of the duodenum, and we found in the superior and posterior margin of the duodenum a small indurated area which we considered to be an ulcer. She had a good deal of dilatation of the stomach, which indicated that in spite of the fact that her stomach may have emptied the barium in a six hour interval there must have been considerable stasis due to spasm of the pylorus.

Further History

Dr. Rose: No ulcer crater could be demonstrated by x-ray, but the findings were considered reasonably characteristic of duodenal ulcer.

In view of the repeated hemorrhages, operative treatment was strongly urged by both the Medical Service and the consulting surgeon. The day after entry she was transferred to the Surgical Service and transfusion of 600 cubic centimeters of blood was done.

On the fourth day she was explored and an ulcer was found on the superior margin of the duodenum. It was quite small and the crater could not be felt through the wall of the duodenum. The whole stomach was enlarged and somewhat thickened. It was transected at the junction of the middle and lower thirds and the distal end was lifted up and freed without much difficulty below the level of the ulcer in the duodenum. The duodenum was then clamped, cut across, and the end carefully infolded. A Polya anastomosis, transmesocolic, was done.

The patient made an essentially uneventful convalescence and was discharged symptom free on the sixteenth day after entry.

Diagnosis

Acute ulcer of the duodenum.
Multiple erosions of the stomach and duodenum.

Pathologic Discussion

Dr. Tracy B. Mallory: On this occasion the resection was so performed as to run below the level of the ulcer in the duodenum, so that no portion of the ulcer was left behind at the time of operation. The specimen which we received showed four or five small erosions and one rather small ulcer.

Dr. Allen noted at the time of operation that the crater was so small he could not get his finger into it. It was in our specimen a rather linear shallow ulcer one centimeter and a half in length and half a centimeter in width. The sections from these areas show fairly acute ulcerations and no other chronic process. So on seeing the specimen the question came up in our minds whether this woman with twelve years of bleeding with eight massive hemorrhages, instead of having a chronic duodenal ulcer, which one might be led to believe from the story, had not perhaps had a succession of ulcers each of which had evidently healed but had been followed after a relatively short period of time, sometimes six months, sometimes three years, by another ulcer. Do you feel that that was within the limits of possibility, Dr. Allen?

Dr. Allen: I certainly think that is a very good explanation for the type of lesion we found. I wondered whether or not you were going to say that she might have bled from her gastritis rather than from her ulcer.

Dr. Mallory: She had a very severe grade of gastritis, but she had a definite enough ulcer, so that I should not think we need assume that the bleeding came from anywhere else.

Have you anything to say about it, Dr. Bradley?

Dr. John I. Bradley: I should agree that the ulcer would offer an adequate explanation for the bleeding here, although it has been demonstrated that gastritis can cause marked and, I believe, even fatal hemorrhage in the absence of ulcer.

Dr. Mallory: I do not think that the question whether it was an acute or a chronic ulcer probably made very much difference in the indication for operation in this case. It was fairly obvious that she had had so many attacks that she was due for a great many more, and medical treatment had been ineffective, so that surgery was the logical thing to try.

Dr. Allen: Surgically in these bleeding ulcers it is not necessary actually to resect that portion of the duodenum involved, although we do so when it can be done safely. It is however important to resect the distal third of the stomach which we believe contains the cells that activate acid secretion. The experience in some European clinics would seem to indicate that the greatest protection against recurrence of peptic ulcer is brought about by resection of the distal third of the stomach. The ulcer in the duodenum, if left behind, would certainly heal providing the acid activating cells were removed and the ulcer area shut off from the irritation of acid and food.

Journal of Medicine

SUCCESSOR TO
THE BOSTON MEDICAL AND SURGICAL JOURNAL

Established in 1828

Published by THE MASSACHUSETTS MEDICAL SOCIETY under the jurisdiction of the

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SUBSCRIPTION TERMS: *$6.00 per year in advance, postage paid for the United States, Canada $7.04 per year, $8.52 per year for all foreign countries belonging to the Postal Union.*

Material for early publication should be received not later than noon on Saturday. Orders for reprints must be sent to the Journal office, 8 The Fenway.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to The New England Journal of Medicine, 8 The Fenway, Boston, Mass.

THE SEASON'S GREETINGS

WHETHER the present impending Christmas and its almost concomitant New Year will fill the doctors' stockings with other than new holes to be darned by patient wives and dutiful daughters continues to be a matter for speculation. Hope, however, still springs eternal in the human breast and there is just a whisper among the remaining leaves of yesteryear that perhaps this hope is not wholly unjustified. The cycles of nature and even of man's attempts to condition natural phenomena are in general rhythmic; regardless of an occasional dropped beat, an extra systole, a touch of heart block or a temporary fibrillation, the pulse of nature continues to force the sap of new life through the arterial tree. There is no more now a status quo than there was in the Year of Our Lord nineteen hundred and twenty-nine, nor will there ever be, so far as history and prophecy can tell. Behind the crest of every sea there comes a trough and every trough is followed by a crest as surely as the ebb tide is succeeded by a rise, despite the efforts of any wet-footed Canute to defy it.

The wind, nevertheless, may shift its direction, and tillers must be changed and sails trimmed to catch it if we would continue on an appointed course under natural forces; bellows may conceivably be set up on the main deck sufficiently powerful to fill the sails, but there is as yet no evidence that they produce any material progress. It is in times of stress and perhaps of discouragement that we must look to the sailing of our vessel, not confusing real seamanship with any idle blowing on the canvas.

For the physician, much or little as he may have needed it, there has been no political Santa Claus to tuck a recovery program in the toe of his stocking or to hang a civil works package on a branch of his Christmas tree. Perhaps the best present that he could have received has been his right to continued independent action; the point is worth arguing. In times of continued economic embarrassment, various difficulties and divers temptations may harass the soul; the temptation to cut a slice from the golden apple if it should roll our way; the danger of trying to hold too long to the old course if the wind has really shifted.

As a New Year's resolution, then, let us avoid alliances that are too entangling and precedents that are too binding, and let us put not too much faith in the easy promises of politics. In our stockings, on Christmas, may we find not too many holes; may we find a small package still of continuing independence, considerable faith in the future and in our own profession, and if the dollars are few may they at least be sound ones.

RHEUMATIC INFECTION IN CHILDHOOD

RHEUMATIC infection with cardiac involvement is the greatest cause of chronic crippling disease in the children of Massachusetts. In spite of the constant study of the disease its etiology remains unknown and its effective therapy limited to little more than was available a hundred years ago. Pathology, epidemiology, and the refinements of biochemical technique are being used in investigations of the infection and new pathways are becoming plain. But the care of the children already affected is difficult and at times disheartening. These children are most often from families economically of the "clinic" stratum and the prolonged care of chronic disease in this group is complicated by financial stress.

In the Children's Cardiac Clinic at the Massachusetts General Hospital the Social Service organization is such that a fairly close touch can be kept with children who are forced by persistent or recurrent infection to remain for weeks or months in bed at home. The parents of these children are instructed, by the doctors

in charge of the clinic and through mothers' meetings, in the meaning of "rheumatism". Emphasis is placed by repetition upon the necessity for being on the constant lookout for evidence of activity of the infection because in childhood it is the activity of the process in the body and not the mechanical damage to the heart that determines the duration of bed rest and the immediate prognosis.

The Committee for the Home Care of Children with Heart Disease at the Massachusetts General Hospital in coöperation with the New England Heart Association have recently published a fifteen page booklet "Short Lessons for 'Rheumatic Families' ", which is to be available for physicians and clinics caring for children with rheumatic infection. In very simple language it discusses the definition of rheumatic fever, rheumatic heart disease and chorea. It describes the rather vague but exceedingly important relationship between respiratory infection and rheumatism, outlines important danger signals of the disease and explains the reasons for rest periods which children so vehemently resist. The lessons end with a few positive and negative instructions about discipline and hygiene. The final section consists of a list compiled by the Boston Public Library, of books containing the biographies of successful men and women who have triumphed over the handicap of chronic disease, such as Theodore and Franklin Roosevelt, Trudeau, Helen Keller, Beethoven, Edison and Robert Louis Stevenson. A few stories for children are also included.

The booklet avoids so far as possible the strictly medical aspects of the rheumatic disease to prevent domestic dosing or the development of neuroses from limited medical knowledge. Its sponsors hope that it may be of value in the practical handling of "rheumatic" children with all their problems of home and school adjustment, and in the explanation to distracted parents of what is expected of them in the care of the child.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

PATTERSON, DANIEL C. M.D. University of Maryland 1906. F.A.C.S. Attending Surgeon, Bridgeport Hospital. His subject is "Appendices Epiploicae and Their Surgical Significance with Report of Three Cases." Page 1255. Address: 881 Lafayette Street, Bridgeport, Conn.

BLUMGART, HERRMAN L. B.S., M.D. Harvard University Medical School 1921. Associate Professor of Medicine, Harvard University Medical School. Visiting Physician and Director of Research, Beth Israel Hospital. His subject is "The Physiology of the Pulmonary Circulation." Page 1259. Address: 330 Brookline Avenue, Boston.

ROESLER, HUGO. M.D. Medical School, University of Vienna 1924. Associate Professor of Roentgenology and Associate Professor of Medicine, Temple University Medical School, Philadelphia. His subject is "Roentgen Study of the Pulmonary Circulation in Health and Disease." Page 1261. Address: Temple University Hospital, Broad and Ontario Streets, Philadelphia, Pa.

WHITE, PAUL D. M.D. Harvard University Medical School 1911. Physician, Massachusetts General Hospital. Address: Massachusetts General Hospital, Boston. Associated with him is

BRENNER, OSCAR. M.D. Birmingham, England. Physician, Queen's Hospital, Birmingham, England. Rockefeller Fellow. Address: Birmingham, England. Their subject is "Pathological and Clinical Aspects of the Pulmonary Circulation." Page 1261.

CUTLER, ELLIOTT C. M.D. Harvard University Medical School 1913. F.A.C.S. Surgeon-in-Chief, Peter Bent Brigham Hospital. Moseley Professor of Surgery, Harvard Medical School. His subject is "Pulmonary Embolectomy." Page 1265. Address: Peter Bent Brigham Hospital, Boston.

CHRISTIAN, HENRY A. A.M., LL.D., Sc.D., M.D. Johns Hopkins University School of Medicine 1900. Physician-in-Chief, Peter Bent Brigham Hospital, Boston. Hersey Professor of the Theory and Practice of Physic, Harvard Medical School. His subject is "Types of Edema and Their Treatment." Page 1267. Address: Peter Bent Brigham Hospital, Boston.

KAPLAN, BORIS. M.D. Saratov University (Russia) 1918 (Formerly Emperor Nicolas II University). Assistant Visiting Physician, St. Luke's Hospital, New Bedford. His subject is "A Case of Gastric Syphilis Simulating Carcinoma of Stomach." Page 1270. Address: 334 Pleasant Street, New Bedford.

PATTERSON, ROBERT L. A.B., M.D. Harvard University Medical School 1932. Intern in Orthopedics, Children's Hospital, Boston. Address: Children's Hospital, Boston. Associated with him is

JONES, CHESTER M. A.B., M.D. Harvard University Medical School 1919. Physician, Massachusetts General Hospital. Assistant Professor in Medicine, Harvard Medical School. Address: Massachusetts General Hospital, Boston. Their subject is "Observations on the Use of Paraffin Oil Preparations." Page 1275.

MACOMBER, DONALD. A.B., M.D. Harvard University Medical School 1909. F.A.C.S. Research Fellow in Obstetrics, Harvard Medical School. His subject is "Studies of Reproduction in the Rat. IV. On the Occurrence of Spontaneous Amputation in Young Growing Rats Whose Mothers Were on Certain Diets." Page 1277. Address: 321 Dartmouth Street, Boston.

MCKITTRICK, LELAND S. B.S., M.D. Harvard University Medical School 1918. F.A.C.S. Surgeon-in-Chief, Palmer Memorial Hospital. Surgeon, New England Deaconess Hospital. Assistant Visiting Surgeon, Massachusetts General Hospital. Instructor, Courses for Graduates, Harvard. His subject is "Amoebic Abscess of the Liver Without Preceding Diarrhea." Page 1280. Address: 205 Beacon Street, Boston.

HURWITZ, DAVID. S.B., M.D. Harvard University Medical School 1929. Research Fellow in Obstetrics, Harvard Medical School. His subject is "Toxemias of Pregnancy. A Critical Review of the Recent Literature." Page 1281. Address: 221 Longwood Avenue, Boston.

THE DEDICATION OF THE MALLORY INSTITUTE OF PATHOLOGY

THE formal opening and dedication of the Mallory Institute of Pathology was held at the Boston City Hospital on Wednesday afternoon, December 13th. Mr. Joseph P. Manning, Chairman of the Board of Trustees, was the presiding officer. After the invocation by Reverend Father John S. Dugan, Dr. Timothy Leary, Medical Examiner of Suffolk County, South, traced the development of the Pathological Laboratory from the early days when all work was done in a small room connected with the boiler house, up to the present. He reviewed, briefly, the contributions to medical science which have been made by the Pathological Laboratory and other laboratories of the institution and emphasized the importance to any large hospital of adequate laboratory facilities, both for routine and investigative work. Mayor James M. Curley reviewed Dr. Mallory's various activities and accomplishments during his connection with the hospital for over forty years and held them up as an example of the highest order of service and self-sacrifice that an individual can render to his fellow-men. Dr. Frank Burr Mallory expressed his appreciation of the honor conferred upon him in naming the building, and outlined the functions of a pathological laboratory. Following the benediction by Reverend Fred K. A. Reeve, the building was inspected by the invited guests.

The Mallory Institute of Pathology, containing over one million cubic feet of space, houses not only the pathological, bacteriological and serological units of the hospital but also provides facilities for the medical examiner of Suffolk County, South, and contains the new ambulance station.

That evening a dinner was given for Dr. Mallory at the Harvard Club. Following the dinner, speeches were made by Mr. F. C. Hood, representing Dr. Mallory's class at Harvard College, Dr. Elliott C. Cutler, representing the surgical profession, Dr. Hans Zinsser, representing bacteriologists, and Dr. James Ewing of New York, representing pathologists. Dr. S. Burt Wolbach was toastmaster and during the course of the evening read letters and telegrams of congratulation received from all parts of the country. At the conclusion, Dr. Mallory was presented with a complete moving picture outfit and a silver pitcher as tokens of the esteem of his former pupils and his friends on the occasion of his retirement and the dedication of the building.

BOSTON MEDICAL LIBRARY

BIBLIOGRAPHIC COURSE

DURING the months of January and February 1934, the Boston Medical Library will give a short course upon Medical Bibliography primarily designed to introduce medical students to the methods employed in prosecuting an investigation of medical literature, acquainting them with the sources of information and the technique of following through a research. Incidentally, sidelights will be thrown upon the history of the art of printing. So far as possible, the course will be a practical one, the resources of the Library being called upon to illustrate the conduct of the course, those who attend being brought intimately in touch with the real technical part of bibliographic study.

The Library hopes in this way to render a service to the schools and to the medical student early in his career, helping him to become more conversant with one of the most valuable aids he may rely upon—keeping abreast of the progress in his profession and establishing within him a realization that graduation from the medical school should not terminate his student days but rather mark their real beginning.

About January first, the Library is planning a bi-monthly exhibition of current medical literature, in abstract, supplemented in the case of more important articles by the originals. This will be displayed in the Fifield Room and will be for members of the Library only. These are solely for reference and it is hoped will afford an opportunity for those who visit the Library to gain in a short space of time a "bird's-eye" view of the more significant contributions to the art and science of medicine as

they are currently issued. This display will be compiled from the published abstracts of those who have composed the various special articles on "Progress" which appear from time to time in the *New England Journal of Medicine* and elsewhere. This exhibit will be changed fortnightly.

Announcement of the dates, subjects and speakers for the Bibliographic Course will be made in the *New England Journal of Medicine* the first week in January, 1934.

MISCELLANY

BOSTON MEDICAL LIBRARY

Friends of the Boston Medical Library have suggested that the historical source material contained in the various collections in the Library should be exhibited from time to time as opportunities presented themselves.

The first exhibit is now on display at the Library where it may be seen during the hours when the Library is open.

It represents the development of the medical book in manuscript and print and notable examples of the thirteenth, fourteenth and fifteenth centuries will be found on the tables in the exhibition room.

When we speak of classical and medieval medicine and science, it is at once evident that our sources of information concerning these periods must be other than the printed book.

Previous to the printing of block books, in which whole words or ideographs comprised one type, which occurred in China, Corea and Europe in the period from the twelfth to the early part of the fifteenth century; and previous to the invention of printing by movable cast type, about 1450, the only books available were in manuscript form.

The manuscript period of book production may be said to have started with the foundation of the monasteries in 550 A.D. and in a few dozen scattered monasteries the monkish scribes in their scriptoria safeguarded the literature of Europe for more than six hundred years.

In the beginning a manuscript was a rare, precious thing to be carefully guarded but as copies multiplied and collections were formed, there was a gradually increasing demand for books until in the last part of the twelfth century the universities of Paris and Bologna were conducting an organized book business.

In the early part of the fifteenth century, previous to the invention of printing, the manuscript business of Venice, Florence and Paris, outside of the universities, had developed into a flourishing business and there was considerable demand from the people for certain classes of literature. Manuscripts were being produced in constantly increasing quantities and at steadily decreasing costs.

Collectors of fine manuscripts regarded the new art of printing with disapproval at the outset and consequently manuscripts were produced for some time after the printing of the first book although it has been estimated that a manuscript would cost about seventy-five per cent more than one of the early printed books.

Thirteen manuscripts dating from 1250 to just before 1500 A.D. are being shown and particular attention is called to the Viaticus Liber of Constantinus Africanus (1050) which is a most important source for medieval medicine. Constantinus was the first great translator from the Arabic into Latin and his "Viaticus" is made up of translations from Isaac Judaeus, Haly Abbas and other Arabian physicians. It is said that through this text the doctrines of the Arabians were disseminated throughout Europe.

It is the very beautiful Nikolsburg codex written in Italy during the thirteenth century on soft vellum. Also of outstanding importance is the text on fevers by Isaac Judaeus written on vellum, probably at Montpellier, about 1250 A.D.

Avicenna (980-1037) was the most famous scientist of Islam and one of the most famous of all times. He ruled the professions of Western Europe and "his triumph was too complete; it discouraged original investigations and sterilized intellectual life" (Sarton).

His most important medical work is the "Canon," an encyclopedic treatise on medicine. Scholarly research requires texts in Arabic, Hebrew and Latin. A beautiful Arabic manuscript, of Persian origin, dated 1309 will be found among the manuscripts and the first Latin and first Hebrew printed texts are shown with the printed books.

The Library also owns early fifteenth century Hebrew manuscripts of books three and four.

Bernard of Gordon was one of the outstanding physicians of the Middle Ages and he wrote a treatise called the "Lily of Medicine," which was first published in 1480. One of the two Hebrew manuscripts shown is a very fine complete text of the "Lily," dated 1468, and written on paper and vellum in a Spanish rabbinical hand.

A document of great importance is the "Registrum" of Burkhard of Rothenburg, 1477. It is a manuscript list of all the drugs and simples necessary for an apothecary shop.

Such lists are of extreme rarity and only one other is recorded in the history of pharmacy.

The books first printed after 1450 were Latin versions of the Bible and writings of classical and religious authors.

Pollard characterizes the books printed before 1481 as the real incunabula because they are the books which men thought the best worth while to spend their money on multiplying when printing first became available.

The great majority of them represent works which students already knew by use or hearsay, but which had been difficult or costly to obtain in

manuscript form. The number of contemporary writings was comparatively small.

In the present exhibition will be found two broadsides and six books printed before 1481.

Popular broadsides were issued dealing with business, religion, health and disease. Those relating to health dealt chiefly with bleeding, purging, and the pest.

At least one hundred bleeding and purgation calendars were printed before 1501, forty-six of which are before 1481. "Pestblatter" to the number of forty-one were described by Heitz in 1907.

These broadsides are extraordinarily scarce as many are in the vernacular and have been lost or destroyed or worn out by constant daily use by the people.

Most of the surviving broadsides are incomplete or imperfect as they have been rescued from the bindings of early books where they have served the purpose of lining papers and consequently have been trimmed by the binder or suffered from the bending of the hinge of the book. It is most unusual to find a perfect, complete, genuine example of one of these broadsides.

Attention is called to the unique "Pestblatt" of 1473 and the unique bloodletting calendar of 1478. The 1496 calendar with its five "Aderlass" illustrations is interesting.

The first books of medical interest were not distinctly medical treatises but books containing matter of a medical character; such as the "Universal Encyclopedia" of Rhabanus Maurus, Strassburg, before July 20, 1467, said to be the first printed book to contain a chapter on medicine, and Pliny's "Natural History," the first book to contain an extensive treatise on medicine and particularly remedies.

Fourteen important printed books are shown and will be found listed in the appended catalog.

The manuscripts of Isaac Judaeus, Constantinus Africanus, Avicenna, Bernardus de Gordonio, Mesue Junior and Johannes Hispalensis and the Rhazes of 1486 and the Hebrew Avicenna of 1491 are from the new Solomon H. Hyams collection of Jewish medicine.

Manuscripts

XIII Century

Issac Judaeus. Liber de febribus. Latin manuscript on vellum. Southern France, probably Montpellier, about 1250. Gothic characters.

Constantinus Africanus. Viaticus liber. Latin manuscript on vellum. Italy, 13th century. The Nikolsburg codex.

XIV Century

Avicenna. Al Qanûn fi't Tibb (Canon). Arabic manuscript on paper. Persian origin. Dated 1309. Scribe 'Ali ibn' Abdi'llâh at - Tarkhanî. Minute Nashki characters.

Eusebius Cremonensis. St. Augustinus. St. Cyrillus. De morte Hieronymi. De miraculis beati Hieronimi. Latin manuscript on vellum. Late 14th or Early 15th century. Gothic characters.

XV Century

Savonarola, Giovanni Michele. Latin manuscript on paper. North of Italy, probably Ferrara, first half of the 15th century. Humanist hand.

Petrus Hispanus. Pope John XXI. Tesoro de poveri. Italian manuscript on paper. Upper Italy about 1450. Gothic characters. A good copy of a very popular medieval medical book.

Jacobus Carthusiensis. Tractatus de potestate demonum, de arte magica, de superstitionibus et illusionibus eorundem. Latin manuscript on paper. Germany about 1450. Humanist hand. Unpublished.

Bernardus de Gordonio. Lilium medicinae. Hebrew manuscript on vellum and paper. Dated 1468. Translated from Latin by Jequthiel ben Salomo. Scribe: Jeschuah ben David Hakohen. Spanish-rabbinical characters. Antedates the first printed edition by twelve years.

Burkhard of Rothenburg. Registrum simplicium ac compositarum rerum medicinalium. Latin manuscript on paper. Probably Vienna or Salzburg, April 27, 1477. Gothic book hand. Medieval drug lists are of the greatest rarity and only one other manuscript list is recorded in the bibliographies.

Johannes Hugo of Heidelberg. Compendium medicinae. Latin manuscript on paper. Dated March 23, 1491. Written in a humanist hand, probably that of the author. An unrecorded and unpublished medical work.

Mesue Junior. De simplicibus. Grabadin. Hebrew manuscript on paper. Naples, 1495.

Gazius, Antonius. De proprietatibus jejunii. Latin manuscript on paper. Dated 1496. Written in Italy in a scribe's hand. Apparently an unknown and unpublished work of the well-known Paduan physician.

Johannes Hispalensis. Opus Quadripartitum et Isagoge. Almansor. Capitula stellarum. Latin manuscript on paper. Germany, end of the 15th century. Humanist characters. This manuscript differs from the printed version as presenting a purer text, free from interpolations.

Printed Broadsides

Pestblatt. Augsburg, about 1473. A popular broadside depicting the Saints Rochus and Sebastian receiving the supplications of plague victims prostrated at their feet. The text consists of separate prayers to each of the patron Saints. That to Saint Sebastian is quite unknown. Unique broadside.

Almanach auf das Jahre 1478. In German. Printed at Nuremberg about 1477 by Creussner. This is a perfect and complete copy of a unique and hitherto unrecorded "Aderlasskalendar."

Honiger, Jacobus. Almanach ad annum 1494. For

Erfurt. In Latin. Printed at Nuremberg by Hochfeder about 1493. Noted for its illustrations of eclipses of the sun and moon.

Almanach für Oesterreich auf das Jahre 1496. In German. Printed at Nuremberg about 1495 by Hochfeder. A good copy of a very important and rare "Aderlass-kalendar," famous for its five medical illustrations which are intact in this copy.

PRINTED BOOKS

1467 Rabanus Maurus. Opus de Universo. Strassburg, the R printer, before 20 July, 1467. A general encyclopedia of knowledge. The first printed book to contain a chapter on medicine.

1472 Regimen Sanitatis Germanice. Von Ordnung der Gesuntheit. Augsburg, Baemler, 23 April 1472. The first edition of a German tract written for the people and the first medical book in the German language.

1472 Avicenna. Canon. Libri 1 - 5. Strassburg, the R printer, before 1473. First edition. See also: Arabic mss. 1309 and Hebrew text 1491.

1473 Plinius Secundus, Caius. Historia naturalis. Rome, Sweynheym and Pannartz, 7 May, 1473.
Pliny's "Natural History," first published in 1469, was the first printed book to contain an extensive treatise on medicine and especially on remedies.

1478 Celsus, Aulus Cornelius. De medicina. Florence, Laurentius, 1478. First edition.

1480 Jacobus de Dondis. Aggregator de medicinis simplicibus. Strassburg, the R printer, about 1480. First edition. A great encyclopedia of treatment.

1486 Rhazes. Liber dictus Elhavi: El continens. Brescia, Brittanicus, 1486. First edition.

1490 Galen. Opera. 2 v. Venice, Pincius, 1490. First edition. The only collected works of a classical author to be printed in the 15th century.

1491 Johannes de Ketham. Fasciculus medicinae. Venice, Gregoriis, 26 July, 1491.

1491 Avicenna. Canon. Libri 1 - 5. Hebrew text. Naples, 'Azri-'el ben Josef, 9 Nov., 1491. The first and only medical incunabula printed in Hebrew.

1492 Johannes de Gaddesden. Rosa anglica practicae medicinae. Pavia, Birreta, 24 Jan., 1492. First edition. John of Gaddesden was one of the two great English physicians of medieval times. The text of the other, Gilbertus Anglicus, was not printed until 1510. Bernard of Gordon did not practice in England.

1497 Brunschwig, Hieronymus. Das Buch der Chirurgia. Strassburg, Grueninger, 4 July, 1497. First edition of a very important illustrated German book on surgery. Particular attention is called to the added "Anathomia."

1498 Gutierrez, Juliano. Cura de la piedra y dolor de la yjada y colica rrenal. Toledo, Hagenbach, 4 April, 1498. Spanish medical incunabula are excessively rare.

1499 Konrad von Megenburg. Buch der Natur. Augsburg, Schoensperger, 1499. Fine copy of a famous German illustrated work containing chapters relating to medicine.

GRADUATES OF MEDICAL SCHOOLS REGISTERED AND REJECTED

MASSACHUSETTS BOARD OF REGISTRATION IN MEDICINE
REPORT OF MAY 23, 24, 25, 1933, EXAMINATION

Medical School	Number Registered	Number Rejected
Boston University School of Medicine	3	0
College of Physicians and Surgeons, Boston	1	4
Harvard Medical School	5	0
Massachusetts College of Osteopathy	2	4
Middlesex College of Medicine and Surgery	6	19
Tufts College Medical School	5	2
Des Moines Still College of Osteopathy	0	1
Emory	1	0
Georgetown University School of Medicine	0	3
Hahnemann Medical School	0	1
Jefferson Medical College	1	0
Kansas City University of Physicians and Surgeons	0	13
Kirksville College of Osteopathy	1	7
Laval University Faculty of Medicine	0	1
McGill University Faculty of Medicine	2	0
Missouri College of Medicine and Surgery	0	1
Philadelphia College of Osteopathy	1	3
St. Louis College of Physicians and Surgeons	0	2
Syrian Protestant College, Beirut	1	0
Temple University	1	0
University of Montreal	0	1
University of Oregon	1	0
University of Tennessee	1	0
University of Vermont	0	1
University of Rome	0	1
Women's Medical College	1	0
Yale University Medical School	1	0
	34	64

REPORT OF JULY 11, 12, 13, 1933, EXAMINATION

Medical School	Number Registered	Number Rejected
Boston University School of Medicine	11	1
College of Physicians and Surgeons, Boston	3	2
Harvard Medical School	3	0
Massachusetts College of Osteopathy	4	7
Middlesex College of Medicine and Surgery	3	19
Tufts College Medical School	20	1
Chicago Medical College	1	0
Des Moines Still College of Osteopathy	1	1
Emory	1	0
Georgetown University	2	1
Hahnemann Medical School	1	1
Johns Hopkins University School of Medicine	1	0
Kansas City University of Physicians and Surgeons	1	17
Kirksville College of Osteopathy	2	11
Laval University Faculty of Medicine	0	1
Medical College of Virginia	0	1
Philadelphia College of Osteopathy	0	5
Royal University of Naples	0	1
Rush Medical College	2	0
St. Louis University of Medicine	1	0
St. Louis College of Physicians and Surgeons	0	1
South Carolina Medical College	1	0
Tulane Medical School	1	0
University of Albany	1	0
University of Buffalo	1	0
University of Chicago	1	0
University of Michigan	1	0
University of Minnesota	1	0
University of Montreal	0	2
University of Toronto	1	0
University of Vermont	1	0
University of Virginia	1	0
University of Wisconsin	1	0
Vanderbilt University	1	0
Yale University Medical School	1	0
	70	72

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1933

Lobar pneumonia shows considerable increase over November, 1932, and is well above the average for the previous five years.

Whooping cough had the highest November prevalence for at least fifteen years, and measles likewise for five years.

We have had sixteen cases of amebic dysentery with two deaths, all of which gave a history of having been to Chicago within a month preceding onset.

Diphtheria and typhoid fever continued to show month for month their lowest recorded prevalence for this state.

Scarlet fever, while showing nothing remarkable for the state as a whole, has worked out of the metropolitan area into the surrounding cities and towns.

Pulmonary tuberculosis reached its lowest November incidence.

Anterior poliomyelitis, chicken pox, epidemic cerebrospinal meningitis, German measles, mumps and tuberculosis other forms show nothing remarkable.

RARE DISEASES

Anterior poliomyelitis was reported from Fall River, 1; Falmouth, 1; Milton, 1; Sheffield, 1; Springfield, 1; Worcester, 1; Total, 6.

Amebic dysentery was reported from Beverly, 6; Brookline, 1; Medford, 1; Reading, 1; Worcester, 1; Total, 10.

Bacillary dysentery was reported from Danvers, 2.

Encephalitis lethargica was reported from Boston, 1; Northampton, 1; Worcester, 1; Total, 3.

Epidemic cerebrospinal meningitis was reported from Northampton, 1; Norwood, 1; Reading, 1; Wilmington, 1; Total, 4.

Malaria was reported from Methuen, 1; Taunton, 3; Total, 4.

Septic sore throat was reported from Belmont, 1; Boston, 7; Cambridge, 3; Easthampton, 1; Fall River, 1; Lawrence, 1; Malden, 1; Northampton, 1; Norwood, 1; Pittsfield, 1; Swampscott, 1; Wenham, 1; Total, 20.

Trachoma was reported from Lawrence, 1.

Trichinosis was reported from Milton, 1; Newton, 3; Total, 4.

Ophthalmia neonatorum and *suppurative conjunctivitis* was reported from Brockton, 13; Cambridge, 2; Canton, 3; Fall River, 4; Haverhill, 2; Melrose, 1; New Bedford, 3; Springfield, 4; Swampscott, 1; Worcester, 3; Total, 36.

Tuberculosis hilum was reported from Belmont, 1; Boston, 10; Cambridge, 3; Gloucester, 44; Groveland, 1; Lynn, 1; Malden, 2; Milford, 1; Natick, 2; New Bedford, 1; Rockport, 3; Salisbury, 2; Sharon, 1; Somerville, 1; Springfield, 1; Watertown, 1; Total, 75.

Tuberculosis other was reported from Abington, 1; Avon, 1; Belmont, 1; Boston, 7; Brockton, 1; Cambridge, 1; Chicopee, 1; Dartmouth, 1; Dighton, 1; Everett, 2; Gloucester, 1; Groton, 1; Lancaster, 1; Melrose, 1; New Bedford, 2; Newton, 1; Somerville, 1; Springfield, 2; Stoneham, 1; Taunton, 1; Tewksbury State Infirmary, 1; Winthrop, 1; Total, 31.

Typhoid fever was reported from Malden, 1; Somerville, 1; Worcester, 2; Total, 4.

Undulant fever was reported from Adams, 1; Northbridge, 1; Total, 2.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

MONTHLY REPORT FOR NOVEMBER, 1933

Disease	Nov. 1933	Nov. 1932	Average*
Anterior poliomyelitis	6	4	29
Chicken pox	772	1127	1056
Diphtheria	100	160	317
Dog bite	333	315	336
Epidemic cerebrospinal meningitis	4	10	10
German measles	28	25	44
Gonorrhea	571	511	456
Lobar pneumonia	434	191	254
Measles	1085	279	649
Mumps	253	353	361
Scarlet fever	696	1038	853
Syphilis	385	310	244
Tuberculosis pulmonary	295	299	347
Tuberculosis other forms	31	32	44
Typhoid fever	4	11	23
Undulant fever	2	1	—
Whooping cough	1308	396	472

*Average number of cases for November during the preceding five years.

AN ADDRESS BY DR. PAUL YAKOVLEV

Dr. Paul Yakovlev of the Department of Neuropathology of the Harvard Medical School and the Munson State Hospital, spoke on "Neural Mechanisms of Epileptic Seizures" on Monday, December 18, 1933, at the State Hospital for Mental Diseases, Howard, R. I.

DR. SHIRLEY W. WYNNE HAS TENDERED HIS RESIGNATION

The *Wall Street Journal* of December 16 has the following announcement:

Late Friday Dr. Wynne announced his resignation as health commissioner, a post he has held since 1928. Dr. Wynne will apply for a pension.

POSTGRADUATE MEDICAL EDUCATION

Plans are under way in Connecticut for postgraduate medical education similar to those in Massachusetts.

If all of the New England State Medical Societies would enter into coöperative methods, much good would result.

COMPARISON OF DISEASE INCIDENCE IN CONNECTICUT WITH 1932 AND SEVEN YEAR AVERAGE

MONTH ENDING NOVEMBER 11, 1933

Diseases	1933 Week ending Oct. 21	1933 Week ending Oct. 28	1933 Week ending Nov. 4	1933 Week ending Nov. 11	Average cases reported for week corresponding to Nov. 11 for past seven years	1932 Week ending Oct. 22	1932 Week ending Oct. 29	1932 Week ending Nov. 5	1932 Week ending Nov. 12
Cerebrospinal Men.	—	1	1	2	—	—	2	—	—
Chicken Pox	42	50	96	62	81	22	52	76	50
Diphtheria	1	—	9	5	17	1	5	6	5
Dysentery Bacillary	—	—	—	1	—	—	—	—	—
Encephalitis Epid.	—	—	—	—	1	—	—	—	1
German Measles	1	1	1	—	—	—	—	—	—
Influenza	5	3	2	2	3	2	2	—	—
Malaria	—	—	—	—	—	—	—	1	—
Measles	1	5	15	3	22	7	10	2	10
Mumps	32	13	31	43	43	79	41	77	53
Pneumonia (Broncho)	20	30	30	35	19	28	23	24	21
Pneumonia (Lobar)	26	21	31	29	20	26	20	18	17
Poliomyelitis	3	1	3	1	2	—	2	—	—
Scarlet Fever	46	39	53	55	41	32	26	54	50
Septic Sore Throat	2	1	1	1	1	1	—	—	2
Tetanus	—	—	—	1	—	—	1	—	—
Tuberculosis (Pul.)	21	13	23	17	25	26	20	31	11
Tuberculosis (O. F.)	2	1	2	1	2	6	—	5	1
Typhoid Fever	2	1	—	3	3	—	—	4	1
Undulant Fever	1	1	—	1	—	—	—	1	1
Whooping Cough	23	31	29	61	42	66	56	88	40
Gonorrhea	30	26	30	28	34	32	32	27	20
Syphilis	34	42	46	43	40	39	53	43	26

Remarks: No cases of Asiatic cholera, glanders, plague, or yellow fever during the past seven years.

The Massachusetts Medical Society

A LETTER OF INFORMATION RESPECTING FEDERAL EMERGENCY ADMINISTRATION

Dear Doctor:

The State authorities have approved the fee-table arranged by the Massachusetts Medical Society for physicians during their attendance upon such patients as are subsisting upon welfare aid. The plan has been submitted to the Federal Government and, as soon as its approval has been granted, physicians may collect their fees through the Federal Relief Administration. The majority of the District Medical Societies have replied to the president's letter of November 20, 1933, and the unanimity of opinion has established a fee-table which has met with the approval of the State Commissioner of Health, Dr. Chadwick, and the State authorities. The fees are two dollars for a house visit, one dollar for an office visit and twenty-five dollars for an obstetric case including prenatal care. A number of questions have been asked by members of the district societies. A physician who wishes to receive fees for services to those of his patients who are classed as indigent sick must be registered with the welfare organization in his community before and during the time of his care. There is no time limit to his registration and he may withdraw his name at his pleasure. Those of his patients who are receiving welfare aid are likewise registered with the welfare organization and they have the right to call their own physicians as was their custom during prosperity. The indigent sick who are without a regular attending physician may apply to their welfare organization and a physician will be selected in rotation from the list of those physicians who have registered.

Reference to a copy of "Regulations No. 7" as printed in the *New England Journal of Medicine*, November 23, 1933, will give the number of visits permitted by the Federal Relief Administration upon acute and chronic cases and the method of increasing the number when necessary. Physicians who register for relief work will find a reading of the regulations helpful.

As soon as the Federal Relief Administration has recognized our fee-table a notice will appear in the *Journal* and physicians who have registered may then collect their fees for attendance upon the indigent sick by presenting their bills to the welfare organization in their community.

Very truly yours,

WILLIAM H. ROBEY, M.D., *President.*

RECENT DEATHS

WILLIS — CHARLES AUSTIN WILLIS, M.D., of 562 Main Street, Waltham, died at his home December 10, 1933. He was born in Waltham, October 26, 1870, the son of the late Dr. John W. and Susan Emily (Rice) Willis. He graduated from Tufts College with the degree of bachelor of philosophy in 1892 and received his M.D. degree from the Harvard University Medical School in 1897. He served as house officer at the Cambridge Hospital and was associated with his father in medical practice until the death of the latter.

He was visiting physician and trustee of the Waltham Hospital, physician to the Waltham Baby Hospital and a trustee and instructor of the Waltham Training School for Nurses. He was medical inspector of the Waltham Board of Health, a member of the Massachusetts Association of Boards of Health and the Waltham Medical Club. He joined the Massachusetts Medical Society in 1898, and was a Fellow of the American Medical Association. He was a Mason.

He is survived by his widow Mrs. Grace E. (Brown) Willis, and a brother Dr. Dwight F. Willis of Boston.

DENNING — WILLIAM EDWARD DENNING, M.D., of Worcester, Massachusetts, died suddenly in his automobile December 7, 1933.

He was born in Burlington, Vermont, in 1872 and graduated from the University of Vermont Medical School in 1899. He served on the Staff of the Worcester City Hospital and for several years on the out-patient staff of the Memorial Hospital. He was consultant to the Fairlawn Hospital, Webster District Hospital and Memorial Hospital in Southbridge. He was a Fellow of the Massachusetts Medical Society and the American Medical Association. He had served as president of the Worcester District Medical Society and represented this Society as a member of the Council of the Massachusetts Medical Society. He was a member of the American College of Surgeons and the American Obstetrical and Gynecological Society.

He was a lieutenant in the Medical Corps during the World War, serving first on the draft board in Worcester, later at Utica, N. Y., at Fort Benjamin Harrison, Indiana, Camp Taylor in Florida and for eleven months at Base Hospital 113 in France. He was a member of the Worcester Club, the Worcester Country Club, and a communicant of Our Lady of the Angels Church.

He is survived by two sisters, Mrs. Katherine Wood of Montreal and Mrs. Mary Triebel of Burlington, Vermont; also three nephews, Harold and George Wood of Montreal and William J. Denning of Worcester.

BRANT — AUSTIN BRANT, M.D., of 407 Beacon Street, Boston, died December 15, 1933. He was born in 1881. He was a graduate of Boston University, and received his medical degree from the Harvard Medical School in 1907. He was trained

at the Boston City Hospital and the Boston Lying-In Hospital, and practiced obstetrics.

He joined the Massachusetts Medical Society in 1909, and was a Fellow of the American College of Surgeons and the American Medical Association.

During the World War he was a reserve officer in the medical corps of the United States Navy. In 1925 he was master of the Gate of the Temple Lodge of Masons.

Dr. Brant is survived by his widow the former Miss Lille Pattengill of Lansing, Michigan, his father the Rev. John F. Brant of Newtonville, and four sisters, Mrs. Fred W. Rust, Mrs. Frederick C. Eaton, Miss Carlotta Brant, and Miss Pauline Brant.

McCABE — CHARLES PENNY MCCABE, M.D., assistant physician on the staff of the Norfolk County Tuberculosis Hospital, died at the Deaconess Hospital, December 15, 1933.

He was born in Canada in 1894, and graduated in medicine from the McGill University Faculty of Medicine, Toronto, in 1919. Before coming to Massachusetts he practiced in North Berwick, Maine. He joined the Massachusetts Medical Society in 1932, and was a Fellow of the American Medical Association.

NOTICES

DR. F. M. BROWN JOINS THE STAFF OF THE RING SANATORIUM AND HOSPITAL

Dr. F. Manning Brown, formerly Fellow of the Mayo Clinic and more recently internist at The Clinic, Honolulu, T. H., has become a member of the resident staff of the Ring Sanatorium and Hospital.

UNITED STATES CIVIL SERVICE EXAMINATIONS

The United States Civil Service Commission announces the following-named open competitive examinations:

Toxicologist Positions

Applications for toxicologist positions of various grades must be on file with the U. S. Civil Service Commission at Washington, D. C., not later than January 11, 1934.

ANNOUNCEMENT

BENJAMIN BANKS, M.D., announces the opening of an office at 475 Commonwealth Avenue, Boston.

RADIO HEALTH MESSAGES

DECEMBER, 1933

HEALTH MESSAGES

Sponsorship: Public Education Committee of the Massachusetts Medical Society and Massachusetts Department of Public Health.

Courtesy WBZ. Fridays, 4:30 P.M.

Dec.

22 Cancer of the Intestinal Tract

29 Preventive Medicine from Your Family Physician

STATE HOUSE BROADCAST

Sponsored by the Massachusetts Department of Public Health.

Courtesy WEEI. Fridays, 1:15 P.M.

Health Subjects of Public Interest discussed by the Division Directors of the Department.

RADIO HEALTH FORUM

Queries from the public are answered under the sponsorship of the Department of Public Health.

Courtesy WEEI. Fridays, 5:00 P.M.

Questions on Health and Prevention of Disease may be sent to Radio Health Forum, State Department of Public Health, State House, Boston.

REPORTS AND NOTICES OF MEETINGS

AMERICAN FEDERATION OF ORGANIZATIONS FOR THE HARD OF HEARING

The Fourteenth Annual Meeting of the American Federation of Organizations for the Hard of Hearing was held in Chicago, June 19 to 22, 1933. In spite of the depression the large attendance and a program of unusual interest made this conference one of the most successful yet held.

The purposes of this organization are of peculiar interest to the practicing physician, especially to the otologist, for, without overlapping the field of his activities, they cover the ground from where the efforts of the medical man usually cease to be effective. The Federation was founded by Dr. Wendell C. Phillips, to improve the condition and to offer relief to persons whose hearing has been lost or impaired; to stimulate and promote all approved scientific efforts in the prevention of deafness, and the conservation of hearing, especially in children. The means for attaining these objectives include the encouragement of scientific research on the causes and treatment of deafness, and in special methods of instruction; assistance in obtaining employment, the creation of facilities for the development and exchange of ideas, and the general education of the public concerning the problems of the hard of hearing. The field a few years ago was entirely untouched. Much has already been accomplished through the establishment of more than one hundred constituent and affiliated bodies, throughout the United States and Canada, each in its own community administering to the educational, social and economic needs of its members.

The national organization, an incorporated body with headquarters in Washington, D. C., has suc-

cessfully stimulated a widespread interest in the periodic audiometric testing of the hearing acuity of school children, as an effective means of deafness prevention notably in New England; has conducted studies of the deafened child of preschool age, and has rendered a great service in increasing the opportunities of the deafened adult for rehabilitation through instruction in lip reading, through organized effort in obtaining suitable employment for those whose hearing defect has excluded them from many occupations. Many have been shown the importance of equipping themselves with a suitable hearing aid and have been helped financially to obtain such aids.

The programs of the annual meetings have been of great interest to educators, social workers and otologists who have all made valuable contributions to a better understanding of the many problems of this large group. The complete Transactions for each year constitute a valuable reference work and should be found in every library covering the field of otology and the problems of the hard of hearing.

The following papers with their discussion were of special interest at the Chicago meeting:

1. "Unemployment Problems of the Handicapped" was ably treated by Oscar Sullivan, State Director, Reëducation of Disabled Persons, St. Paul, Minnesota. He made an eloquent plea for greater justice to the handicapped, including the deafened, urging that a certain proportion of such be given public positions by various Federal, State, County and Municipal agencies, through special legislation for this purpose. He cited a beneficent law passed in Minnesota in 1919, providing for the reëducation of the handicapped.

Such legislation would go far to a greater recognition of the possibility of satisfactorily employing more of the adequately trained handicapped in industry generally. Placement should be a part of rehabilitation. He placed much hope in the future activities of the proposed National Council for the Handicapped to coördinate the activities of many interested social and welfare organizations.

Miss Edith Katz of the Employment Bureau of the New York League for the Hard of Hearing, discussing the paper, made the very pertinent suggestion that in the case of the deafened, the matter of placement was equally important with rehabilitation and training. She advocated state legislation along the line suggested by the reader of this paper.

Dr. Martin Hayes Bickham, Director of the Illinois Emergency Relief Commission, stressed the question of social injustice now facing the handicapped workers in America. He stated that in his belief twenty per cent of the unemployed workers have a handicap. These should be put back to work in the same proportion as they bear to the other unemployed.

2. "How the Federation Can Assist in Employment Problems" was presented by Miss Ada Morgan Hill, Director, Federation Department of Vocational Advice. She introduced the subject by quoting from a paper by President Roosevelt written while he was Governor of New York, in which he stated that "One of the great problems for the physically handicapped is to develop a perfectly rational attitude toward their own disabilities, their problems and the world of able-bodied people. The elimination of self-pity, on the one hand, and undue pride and embarrassment on the other, is most important and goes a long way toward minimizing any handicap, even an extremely severe or incurable one. At the same time it is most important to educate the public at large to a comprehensive understanding of physically handicapped individuals, their reactions and their problems."

The Federation should exercise a strong influence in the employment problems of the hard of hearing throughout the country. Since 1924 through its Department of Vocational Advice the Federation has made large efforts to help the individual applicant.

The Federation has long sought to mold public opinion in the direction of creating a favorable attitude of employers toward the hard of hearing.

It is recommended that a definite program be devised to unite the various forces working for the handicapped by creating a favorable public opinion and ultimately securing better legislation to meet these needs of the handicapped.

Miss Hill's fine analysis of the situation was commended by Tracy Copp, Regional Agent, Federal Board of Vocational Education, Washington, D. C. He restated the situation in the following words: "Preparing a disabled person for employment is a scientific process which consists of:

1. A survey of the case.
2. The selection of a vocation.
3. Preparation for the selected vocation.
4. Supervision during the entire period of rehabilitation.
5. Placement in employment.
6. Follow-up in employment until rehabilitation is assured.

The social adjustment of the hard of hearing person is a process in which only those who have lost their hearing can be properly and sympathetically helpful. He recommended that workers in employment offices for the handicapped carry on scientific studies of industrial changes.

3. "The Relation of the Various Federation Activities to Health" was presented by Dr. Wendell C. Phillips of New York. He stated that health is the "quality of life that renders the individual fit to live most and serve best". He emphasized the fact that health is something more than what is simply related to physical well-being, in that it enables one to live most and best, and to realize his potentials.

He applies this conception to the various activities of the Federation. Supplying a person out of work because of the handicap of deafness, with gainful occupation, will restore his health by relieving him

of his worries and despondency and transform him from an isolated, depressed, unhappy introvert into an individual with normal interests, self-confident and capable of taking his rightful place in the world.

The conservation of hearing among school children as urgently advocated by the Federation by the early discovery of hearing loss and the application of corrective measures, is a health measure of a high order. Likewise the Federation's encouragement in the improvement of hearing aids and their employment by the hard of hearing, whereby they are given opportunity to enjoy normal social and educational contacts, is an activity for health.

The Federation also carries on a vigorous, national campaign for proper aural hygiene to conserve the hearing, to make the public more ear conscious and give better care to the hearing organ.

Its exhibits at various national, state and local scientific gatherings are highly educational along the line of hygiene of the ear and in the field of rehabilitating the deafened.

The protection of the hard of hearing against being victimized by quackery in many forms is another effective health activity of the national organization.

A noteworthy activity of the Federation is that of the Everywhere League, through which a large number of isolated deafened individuals are reached by correspondence. These persons are given advice and encouragement in the solution of their individual health and other problems related to their handicap. Dr. Wm. F. Snow, New York, in discussing Dr. Phillips' paper pointed out the need of considering from a health point of view the hard of hearing individual as a whole.

4. In the scientific session, Dr. Edmund Prince Fowler, of New York, contributed a paper on "Variations in Hearing with Otosclerosis." His material consisted of one hundred and twenty-eight cases of otosclerosis, half of them private patients and half cases studied in the clinic he conducts in the Manhattan Eye, Ear, Nose and Throat Hospital for the New York League for the Hard of Hearing. Changes in the hearing amounting to ten sensation units or more at several frequencies occurred in fifty-one cases. With hardly an exception a cause for such variations could be found in the middle ear. This cause operated to increase the deafness caused by the otosclerosis.

A large percentage of these cases both with and without a complicating nerve deafness showed evidence of past inflammation in the middle ear. Further, he stated, that in forty cases of otosclerosis studied by serial microscopic sections, and on twelve studied by individual slides, there was evidence of inflammatory lesions in the middle ear. More than half of the one hundred and twenty-eight cases gave no history of inflammatory disease of the middle ear.

A distinct history of colds was obtained in sixty-two to eighty per cent of all cases uncomplicated by nerve deafness. He makes the following points: First: Otosclerosis seldom occurs without other lesions in the ear. Secondly: The first symptoms of otosclerosis are often the symptoms of the other complications noted. Thirdly: Improvements in hearing are due to improvements in these complications and not to the otosclerosis itself. Fourthly: Losses in hearing are often due to these complications and not to an increase in the otosclerotic process. Fifthly: Treatment is legitimate and is indicated for these complications. Sixthly: We know of no efficient treatment for otosclerosis itself. Seventhly: We cannot ignore the almost universal presence of past inflammation of the middle ears of otosclerotics.

The author is of the opinion that the only approach to treatment of otosclerosis which promises arrest of the lesions is treatment to combat the tendency to recurrent or chronic inflammatory processes in the nose or ear spaces, particularly the nasal sinuses.

In the discussion of this paper, Dr. George Shambaugh, Jr., Chicago, disagreed with the author as to the causal rôle played by previous inflammatory disease of the middle ear in children in producing otosclerosis.

CLINICAL STAFF MEETING OF THE MASSACHUSETTS GENERAL HOSPITAL

On Thursday evening, November 16, the Clinical Staff of the Massachusetts General Hospital held a meeting in the Moseley Memorial Building. Dr. William B. Robbins presided, and the topic for discussion was Hyperparathyroidism.

Dr. Fletcher Colby read the first paper on "Renal Calculi in Association with Certain Diseases of the Parathyroid Gland." The speaker stated that stones in the urinary tract constitute a symptom rather than a disease, for there are any number of causes of this condition. Normal urine is a supersaturated solution of the salts it contains. The reason that these salts are held in solution is that there is a protection of the molecules by colloidal membranes. If urine is allowed to stand, some of the molecules coalesce and form a precipitate which can be dissolved only with difficulty. If the crystalline content of urine is increased, the colloids may be unable to hold them in suspension and there may be a precipitation taking place in the urinary tract. The conditions leading to this deposition of crystals vary, and in some instances urate crystals are deposited, in others oxalate crystals.

Obstruction along the urinary tract seems to favor a deposition of salts from the urine, as does infection. Recently it has been shown that a diet deficient in vitamin A predisposes toward renal lithiasis, and in such instances the calcium stones are most common. Because of the increased urinary output of calcium in hyperparathyroidism, stones were found in 65 per cent of the cases studied at this hospital. It has also been shown experimentally that animals develop renal calculi if

given large doses of parathormone, and in those cases where the added factor of urinary stasis was produced together with hyperparathyroidism, 38 per cent of the animals showed stones.

Of the 13 cases of parathyroid tumor studied at the Massachusetts General Hospital, three of the patients entered with a complaint referable purely to the presence of renal calculi, and there were no other symptoms of osteitis fibrosa cystica. For this reason, routine examinations of the serum calcium and phosphorus are now done at this hospital in cases of renal lithiasis.

In conclusion Dr. Colby presented two case histories. The first was that of a 22 year old Italian shoemaker, who entered the hospital with a complaint of hematuria and pain in the right kidney region. Seven months previously he had had pain in the right flank radiating to the right testicle, and had passed a stone after a cystoscopic examination. The pain continued until entrance when tenderness in the right kidney, a slight trace of albumin and red blood cells in the urine were found. The pyelogram showed a calculus in the pelvis of the right kidney. The blood calcium at this time was 15.8 mgs. per cent and the blood phosphorus 2.9 mgs. per cent. At separate operations, the renal calculus and a parathyroid tumor were removed.

The second patient was a 51 year old, married woman, who had had her left kidney removed 11 years previously for extensive lithiasis. Three years before entry a stone was removed from her right kidney, a recurrence of which was found. Her serum calcium was 12.5 mgs. per cent and the phosphorus 2.19 mgs. per cent. Because the stone was impacted, giving complete anuria, an emergency nephrostomy was performed. During the following weeks the stone progressed down the ureter until it could be felt by vagina. Although no stone was passed, there was none to be found after the parathyroid tumor had been removed.

Dr. Fuller Albright spoke on "Medical Manifestations of Parathyroid Disease." The speaker began with some general remarks on calcium metabolism in the body. The fluid of the body tissues contains calcium in an almost saturated solution. If calcium is added to the tissue fluids, some in turn goes into the bones to reëstablish the delicate equilibrium. On the contrary, calcium removed from the tissue fluids leads to a decalcification of bone to make up the deficit. The diet is the source of the calcium used in the body; while the G.I. tract and kidney both play a part in its excretion.

The speaker next showed some slides depicting the increased activity of the osteoblasts and osteoclasts in this disease. The unusual activity of these builders and destroyers of bone indicates that in osteitis fibrosa cystica there is a constant destruction and reformation of bone going hand in hand. Because the osteoclasts require a heavy connective tissue support, fibrosis is commonly found in the bone marrow. The unusual activity of the osteoclasts sometimes leads to the formation of benign giant cell tumors. When several adjacent areas of osteoclastic activity coalesce, a cyst is formed. The thinning of the bony cortex leads to a weakening of the bone and hence spontaneous fractures are common. These four conditions, fibrosis, giant cell tumor, cysts, and fractures, are all explained on the basis of the osteoblastic and osteoclastic activity.

The symptoms of the disease are just the opposite of those seen in tetany. The patient is slow in his reaction time and feels tired. Constipation is common, and because of the laxity of the tendons, flat feet are frequently seen. The structural changes in the skeleton lead to pain and tenderness over the bones. Polydipsia and polyuria are often seen as a result of increased excretion of calcium by the kidney.

Dr. Albright next explained the different types of cases which one finds in hyperparathyroidism.

A. This type shows chiefly skeletal changes and is marked by bone cysts and great deformity in the bony framework. The kidney may also show stones as a result of increased calcium excretion.

B. The osteoporotic type shows marked decalcification of the bone but no cysts, tumors or fractures. The so-called "fish vertebrae" are common as a result of the expansion of the nucleus pulposus made possible by the great thinning of the vertebrae.

C. In patients with a high calcium intake, the bony framework is little affected and nephrolithiasis is the predominant feature.

D. Some patients have shown typical signs of Bright's disease with renal insufficiency. In these the calcium deposits were multiple and were scattered throughout the kidney substance.

E. There have been no examples of this type at the Massachusetts General Hospital, but the patients show signs of toxicity and die rapidly just as animals do when they are given overdoses of parathormone. In these instances calcium deposits are found in the kidney, the alveoli of the lung and the mucosa of the stomach.

F. Recently a patient has been found who shows definite blood changes of hyperparathyroidism, but who as yet shows no symptoms. Her bony skeleton manifests the typical thinning of the cortical structure.

It is possible for patients to have this disease for a long time. One woman had a crushed vertebra 39 years previous to her entrance for the removal of a bladder stone, when the disease was discovered. By a high intake of calcium she was able to maintain a good equilibrium.

The phosphatase level in the blood stream may be normal in hyperparathyroidism. It is thought that this enzyme is liberated by the osteoblasts and is capable of converting organic calcium into the inorganic form.

Dr. Albright stated that Paget's disease and hyperparathyroidism are quite distinct conditions. Paget's disease is a localized process as was well illustrated by lantern slides, while osteitis fibrosa cystica involves a general thinning of the bones as one would expect from a hormonal oversecretion. In no case of Paget's disease has a tumor of the parathyroid glands been found; while from all the cases diagnosed as hyperparathyroidism a tumor has been found at operation.

Although recalcification of bone is possible by a high calcium diet, surgery is the only certain cure for this condition and should be used in every case so diagnosed.

Dr. E. D. Churchill spoke on "The Surgical Treatment of Parathyroid Tumors." These tiny glands may lie anywhere in the neck anterior to the deep cervical fascia as well as in the anterior or posterior mediastinum. In only two of the cases at the Massachusetts General Hospital could a tumor be felt in the neck previous to operation and one of these turned out to be an adenoma of the thyroid. One should not remove normal parathyroid glands in this condition, but should search until he finds the tumor even though it means splitting the sternum. In cases of extensive osteoporosis it is well to do a subtotal resection of the tumor, followed by a total extirpation, in order to avoid postoperative tetany.

Dr. J. C. Aub and Dr. Walter Bauer discussed the papers, after which the meeting was adjourned.

NORFOLK DISTRICT MEDICAL SOCIETY

The Norfolk District Medical Society met on Tuesday, November 28, at 8:15 P.M. in the Masonic Temple, Roxbury. Following a lengthy business session, the meeting was turned over to Dr. Frederick T. Lord, who had been invited to arrange the scientific program. This consisted of three parts, each dealing with a phase of lobar pneumonia. Dr. Roderick Heffron outlined the work being done in the study of pneumonia in Massachusetts by the Committee under the Commonwealth Fund of New York City. Dr. Lord discussed the diagnosis and treatment of lobar pneumonia, and Dr. Robert Linton presented the surgical treatment of empyema.

According to Dr. Heffron, the purposes of the Pneumonia Study in Massachusetts are the following: 1. To study the epidemiology of pneumonia, its transmission and spread. This is being carried out by Dr. Wilson G. Smillie, of the Harvard Medical School. 2. To study and improve the methods of serum production. Drs. White and Robinson, at the Antitoxin and Vaccine Laboratory in Forest Hills, are concerned with this phase of the work. 3. To devise procedures for serum treatment, and administrative measures for the prevention and control of this disease. Dr. Heffron indicated that though the average cost for treatment of a type I lobar pneumonia patient with the concentrated antipneumococcus serum was fifty to sixty dollars, this serum would be given gratis to any physician of the Society, after January 1, 1934, who would be willing to use it according to instructions and to return a short questionnaire properly filled out to the Committee. This is part of the program devised to provide serum free of charge to physicians throughout the State who will coöperate in the Pneumonia Study.

Dr. Lord, in discussing the diagnosis and treatment of lobar pneumonia, stressed the advisability of employing concentrated antipneumococcus serum, types I and II, before the fourth day of the disease. When so utilized, he believes there is great value in this therapy. Not only is the course of the disease shorter and milder, with a prompt drop in temperature, pulse, and respiration, but bacteremia is also likely to disappear following the use of the serum, and there may be cessation in the spread of the pneumonia process. In the case of a patient seen on the fourth day, it is better to treat first and to determine the type at once, to guide further treatment. By the Neufeld method, typing can be accomplished in twenty minutes. Dr. Lord demonstrated the proper technique in the administration of serum, and advised proceeding with caution in patients who have a history of asthma, hay fever, eczema, urticaria, or angioneurotic edema, or who have had previous injections of horse serum.

Dr. Robert Linton next proceeded with a consideration of the surgical treatment of empyema. This most common complication of lobar pneumonia should be looked for, he said, if there is a recrudescence of temperature two to seven days after the crisis. A needle should be introduced into the site of the suspected pus, and the diagnosis thus made definite. He believes thoracentesis is not done enough at the present time, and as no harm is likely to come from such a procedure, it should be carried out when suspicion points to empyema. It is best to tap high, at about the eighth space posteriorly, to avoid a high diaphragm, the result of distention. X-ray is sometimes helpful in localizing the empyema.

The character of the pus and the organisms found on gram staining and microscopical examination will determine the form of treatment to be employed. There are three methods of procedure: repeated aspirations with a fairly large syringe and an air-tight union; closed catheter drainage; rib resection. Repeated aspirations have provoked but few cures. The method is useful in tiding over patients that are very ill. Rib resection should be employed with due caution. Closed catheter drainage under air-tight conditions was recommended as most generally applicable. Not more than a few cubic centimeters of air should be allowed to enter the pleural cavity. Normal saline irrigation of the empyema cavity, Dr. Linton pointed out, is less

apt to induce a prolongation of temperature than would Dakin's solution.

SUFFOLK DISTRICT MEDICAL SOCIETY

The November meeting of the Suffolk District Medical Society was held in the amphitheatre of the Beth Israel Hospital on Wednesday evening, November 29, 1933. Dr. James H. Means, Vice-President of the Society, called the meeting to order and then turned the clinical program over to Dr. Harry Linenthal, who introduced the speakers.

The first paper was by Dr. Charles G. Mixter, Surgeon-in-Chief at the Beth Israel Hospital, on the subject "Regional Ileitis." Dr. Mixter began by reciting a typical history of a patient with this disease. The patient was a twenty year old male who, six months before entry, had been operated on for "subacute appendicitis". A pelvic abscess and a sinus later developed and, on admission to the hospital, examination revealed a discharging sinus at the lower end of a right lower quadrant scar. Fibrosed mesenteric glands were found on exploration, ileostomy was performed, and the fecal fistula finally closed. Following discharge from the hospital the patient had attacks of abdominal pain and anorexia. A gastrointestinal series showed partial obstruction in the region of a stenotic lower ileum.

The speaker then discussed some of the more general aspects of the disease. Crohn, Ginzburg, and Oppenheimer first described the entity about fifteen months ago from the Mt. Sinai Hospital in New York. Since then a few more cases have been reported by other workers. The condition seems to be a clinical but not a pathological entity. There are four stages: (1) signs of acute inflammation in the right lower quadrant, (2) symptoms of an ulcerative enterocolitis, (3) signs of incomplete, partial obstruction due to stenosis of the bowel, and (4) formation of a fistula. Pathologically there is thickening of the wall of the bowel, edema, inflammation, and thickening of the mesentery, with ulceration along its border, and hyperplasia of the neighboring lymph glands. The microscopic picture is not characteristic; the presence of giant cells is suggestive of tuberculosis, but this has never been confirmed by guinea-pig inoculation. Bacteriological findings are not consistent. The disease usually occurs in young adults, in males more frequently than in females. Its course is chronic and measured in terms of months and years. Common findings are fever, diarrhea, pain in the right lower quadrant, loss of weight, anemia, blood and mucus in the stools, and occasionally there is vomiting. On physical examination there is resistance in the right lower quadrant, induration and a palpable mass, and later a fistula. By x-ray there is evidence of partial intestinal obstruction. The lesions to consider in differential diagnosis are tuberculosis, ulcerative colitis, carcinoma, and the rarer granulomata, Hodgkin's disease and actinomycosis. The only satisfactory treatment is surgery; ileostomy first, followed by resection after the patient's general condition improves, or resection with ileocolostomy at the start.

Dr. Linenthal and Dr. Hans Zinsser then presented interesting accounts of Brill's disease, the former presenting the clinical and the latter the bacteriological side. In 1910 Nathan Brill collected 221 cases of a condition which he described as an infectious disease of unknown origin. Though it appeared to Brill to resemble mild typhus fever, he did not believe it to be typhus because it did not seem to be contagious, fatal, or epidemic. In 1912 Anderson and Goldberger, in immunity experiments, showed that Brill's disease and the so-called "Mexican typhus" were identical. Thus came the concept that typhus is endemic in this country. Thirteen cases have been seen at the Beth Israel Hospital during the past five years. The disease is acute in onset, with headache, prostration, chills, generalized pain, and a temperature up to 105 degrees reaching its height on the third day and continuing to the twelfth or fourteenth day, followed by a crisis or rapid lysis. Sometimes a cough and bronchitis accompany the acute stage. From the fourth to the seventh day there occurs a maculopapular rash over the abdomen, back, and extremities, never on the face. The rash does not disappear on pressure. Sometimes the spleen is palpable. The white blood count usually varies between 8000 and 11,000. By the middle of the second week a positive agglutination reaction is obtained with "bacillus proteus X 19" (Weil-Felix reaction). Influenza, meningitis and bronchopneumonia have to be ruled out in differential diagnosis. Recovery is the rule in Brill's disease.

In discussing the bacteriology of the disease, Dr. Hans Zinsser declared that all of the many types of typhus fever overlap in their serological relations and suggested that they all have essentially the same etiological agent, modified perhaps into the various subgroups by animal passage. He described the work going on in his laboratory on the rickettsia bodies and animal passage and carriers, and spoke of the importance of investigating the disease in this country, where the sporadic nature of the occurrence of the disease may make the acquisition of epidemiological knowledge easier than in the severe epidemics of Europe.

The final subject on the program was an account of the recent work at the Beth Israel Hospital on total ablation of the thyroid gland in severe cardiac decompensation and angina pectoris, by Drs. Herrman L. Blumgart and David D. Berlin. Dr. Blumgart first discussed the general physiological principles involved. The most important of these is the principle that the speed of the blood flow in the body is directly proportional to the metabolic rate. In thyrotoxicosis it has long

been known that operation brings about marked improvement in circulatory failure if the latter is present before operation. In myxedematous patients vigorously treated with thyroid, anginal pains and even decompensation may ensue. In the first patient studied in this series subtotal thyroidectomy was done and as the remaining thyroid began to function more adequately and the metabolism rose to normal, the cardiac decompensation again reappeared. From then on total thyroidectomy was effected in a series of patients with cardiac decompensation or with angina pectoris. The fall in the basal metabolic rate seemed to be proportional to the clinical improvement, and strikingly good results have been obtained in a rather large number of cases.

Dr. Berlin discussed the surgical aspects of the problem. The two main features in the operation of total thyroidectomy are, of course, preservation of the parathyroid glands and the recurrent laryngeal nerves. Slides illustrating the operative technique were shown. As a precautionary measure laryngoscopy is performed after one side is done before proceeding with the operation, in order to verify the normal functioning of the vocal cords. Fifty-seven cases of very severe decompensation or angina pectoris have now been operated upon. The anesthetic used has been gas-oxygen or local infiltration. There were four operative deaths in the first 38 cases, and two subsequent deaths from congestive failure. Striking improvement was obtained in most of the other cases. There were eight cases of unilateral recurrent nerve injury; six of paralysis, two of paresis. Eight patients showed chemical evidence of parathyroid insufficiency postoperatively, but only one needed parathormone and only one still requires calcium medication.

At the end of the meeting the staff of the hospital presented a number of apparently hopeless cardiacs that have been greatly benefited by the operative procedure.

FAULKNER HOSPITAL CLINICAL MEETINGS

On Thursday afternoon, December 7, at 5:00 P.M. the regular monthly meeting was held at the Faulkner Hospital.

One interesting case which had come to autopsy was discussed. The patient had been to Chicago in September. Without developing any appreciable symptoms pointing toward the gastro-intestinal tract, he began to have fever and eventually came in to the Faulkner Hospital with evidence of inflammation in the right upper quadrant of the abdomen and some signs pointing toward infection in the lower right pleural cavity. The patient was so ill on arrival at the hospital that death occurred before operation could be decided upon. At the autopsy a very large abscess of the liver was found which was due to amoebae. There were also amoebic ulcerations in the large bowel especially in the region of the cecum and ascending colon. The unusual feature of the case was the presence of these ulcerations in the large bowel without appreciable symptoms pointing toward the gastro-intestinal tract.

Dr. Henry C. Marble then presented a case of staphylococcus pyogenous aureus infection which localized in the head of the right femur and extended to the right hip joint. This was successfully treated by drainage of the joint. The unusual and instructive features in the case were discussed. During the first twenty-four hours in the hospital there was no limitation of motion in the hip joint upon manipulation although the pain was so pronounced that the patient could scarcely move the leg. This was probably due to the beginning osteomyelitis without immediate involvement of the joint. Another interesting feature was the existence of positive blood cultures for several weeks without the organisms localizing in any other spot, with the possible exception of a minute abscess in the urinary tract as suggested by bloody urine for one day. The lack of leukocytosis caused confusion in the diagnosis and delay in operation because it raised the question of acute rheumatic fever with localization in the hip joint. Finally the statement of the roentgenologist two or three days before the operation that the capsule of the joint was distended showed the assistance that the x-ray can give early in these cases. Subsequent studies by the x-ray showed that a suspicious area in the bone was really an osteomyelitis, but the diagnosis could not be positively made on the original film.

Dr. Marble also presented an interesting case in which successful skin grafting had been made by transferring some skin attached by a pedicle from the abdomen to the palm of the hand. The graft was successful and the time had arrived for the pedicle to be detached. Considerable discussion followed in regard to the technique of skin grafting by this method.

Dr. Frederic J. Cotton then presented for discussion a case of fracture of the right os calcis resulting from a fall which had not been reduced. He emphasized the importance of radical reduction in these cases because of the bad results obtained otherwise. The ecchymosis and swelling should first be reduced by compression. Tongs or a pin are then inserted in the back part of the os calcis on which traction is made while the external plate of the bone which is always displaced outward is returned to its normal position by pressure with the thumb, or by a blow with a hammer or with a clamp. The position is then maintained by putting the foot in plaster. Dr. Cotton called attention to the fact that if disability results after good reduction, it is due to overgrowth of bone externally and interference with the posterior joint underneath the astragalus. This excessive bone can be taken care of easily by a subsequent operation. He

favors an arthrodesis of this subastragaloid joint according to Dr. Philip Wilson's technique only in those cases in which motion cannot be preserved. After an arthrodesis nothing further can be done if the results are not entirely satisfactory. Although arthrodesis unquestionably greatly reduces the length of stay in the hospital it seems worth while to substitute a convalescence of several months if by so doing full function may be obtained.

The next meeting will be held at the Faulkner Hospital at 5:00 P.M. on Thursday, January 4. In addition to the usual pathological conference on the cases which have come to autopsy during the month, Dr. W. Richard Ohler will talk on "Recognition and Treatment of Unsuspected Hypothyroidism." All members of the profession are invited to attend.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

It has been announced that at 10:30 A.M., December 28, Dr. Henry E. Sigerist, Director of the Institute of History and Medicine of Johns Hopkins University, will open the Symposium on Sociology and Medicine with the subject "Inter-Relationship of Medicine and General Culture," being followed by Mr. Henry Dennison of Framingham, on "The Relation of Medicine to Social Trends."

The rest of the Symposium will be given by Mr. Douglass V. Brown, Miss Ida M. Cannon and Dr. George R. Minot as stated in the complete program of the Association which appeared on page 1251 of the December 14 issue.

The meetings will take place from December 27 to 30 in the John Ware Hall, Boston Medical Library, 8 The Fenway, Boston.

AMERICAN CONFERENCE ON BIRTH CONTROL

Under the auspices of the National Committee on Federal Legislation for Birth Control, the American Conference on Birth Control will take place January 15, 16, and 17, 1934, at the Mayflower Hotel, Washington, D. C.

The methods advocated, and allied subjects, will be considered, and an effort to mobilize public opinion in favor of federal legislation which will permit suitable agencies to give contraceptive information, will be made.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The Ninety-Third Semi-annual Meeting of the Essex North District Medical Society will be held at the Elks Club Rathskeller, Summer Street, Haverhill, January 3, 1934, at 12:30 P.M.

1:30 Business meeting.

At two o'clock Hon. Richard K. Conant, Commissioner of Public Welfare for Massachusetts, will speak on "The Doctor and Departments of Public Welfare," including a discussion of new federal arrangements for local medical care in the home, followed by a general discussion of local medical welfare problems and recommendations by physicians of Lawrence, Haverhill, Merrimac, Amesbury and Newburyport. Floor discussion limited to 3 minutes.

E. S. BAGNALL, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

December 21—Clinic at the Peter Bent Brigham Hospital at 3:30 P.M. conducted by Dr. Henry A. Christian.

December 21—New England Hospital for Women and Children will hold its regular clinico-pathological conference at 8 P.M.

December 27-30—American Association for the Advancement of Science, Section N (Medical). See page 1251, issue of December 14, also notice elsewhere on this page.

January 4—Faulkner Hospital Clinical Meeting. See notice elsewhere on this page.

January 15, 1934—Boston Medical History Club. Speaker: Professor Henry E. Sigerist, Director of the Institute of Medical History of Johns Hopkins University.

JAMES F. BALLARD, Secretary.
Boston Medical Library, 8 The Fenway, Boston.

January 15, 16, and 17, 1934—American Conference on Birth Control. See notice elsewhere on this page.

February 16 and 17, 1934—The New England Hospital Association is holding its Twelfth Annual Meeting at the University Club, Boston. For details write Dr. A. G. Engelbach, Massachusetts General Hospital, Boston.

April 16-20, 1934—The American College of Physicians will hold its Eighteenth Annual Clinical Session in Chicago at the Palmer House. For information write Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

July 24-31, 1934—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schniz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 4, 5, 6, 1934—International Union Against Tuberculosis will be held in Warsaw. For particulars address The National Tuberculosis Association, 450 Seventh Avenue, New York, N. Y.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH DISTRICT MEDICAL SOCIETY

January 3—See notice elsewhere on this page.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

Wednesday, January 3—Danvers State Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Clarence A. Bonner, Superintendent of Danvers State Hospital. Subject: Recent Experiences in Foreign Clinics.

February 7—Council Meeting, Boston.

Wednesday, March 7—Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Frank H. Lahey, Boston. Subject to be announced. Film Electrocardiogram.

Wednesday, April 4—Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speakers: Dr. Elliott P. Joslin and Dr. Howard F. Root, Boston. Subject: "Tuberculosis Complicating Diabetes."

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.
221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings will be held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings will take place on January 10 at Melrose, March (2nd Wednesday) at Wakefield, and May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.
76 Church Street, Winchester, Mass.

MIDDLESEX NORTH DISTRICT MEDICAL SOCIETY

Meetings will be held on January 31, and April 25 (Annual Meeting).

T. A. STAMAS, M.D., Secretary.
226 Central Street, Lowell, Mass.

NORFOLK DISTRICT MEDICAL SOCIETY

Postgraduate Course. See page 1184, issue of December 7.

January 28—Tentatively Roxbury Masonic Temple, 8 P.M. Continuance of Symposium on Diseases of the Blood. Dr. Dameshek and Dr. Straus.

February 27—Place, time, subject, and speaker to be announced.

March 27—Place and time to be announced. Dr. Edward A. Edwards and Dr. Henry H. Faxon. Symposium on the Treatment of Varicose Veins.

May—Annual Meeting. Place, time and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.
1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

January 4—12 noon at Norfolk County Hospital. Speaker to be announced.

February 1—12 noon at Norfolk County Hospital. Stated Meeting. Speaker: Dr. Sara Jordan. Subject: Stomach Ulcers.

March 1—12 noon at Quincy City Hospital. Program by the hospital staff.

April 5—12 noon at Norfolk County Hospital. Speaker: Dr. Elliott P. Joslin. Subject: Diabetes.

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.
Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

January 31—General Meeting in association with the Boston Medical Library and the Trudeau Society. Speaker: Dr. Lawrason Brown of Saranac Lake.

March 28—Clinical Meeting at the Massachusetts Memorial Hospitals.

April 25—Annual Meeting at the Boston Medical Library. Election of Officers. Scientific Program, titles and speakers to be announced.

The Medical Profession is cordially invited to attend all of these meetings.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary,
311 Beacon Street, Boston, Mass.
ALEXANDER S. BEGG, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

All meetings to be held on Wednesdays as follows:

January 10—Dinner and scientific program at the Worcester City Hospital, Worcester, Mass.

February 14—Dinner and scientific program at the Worcester State Hospital, Worcester, Mass.

March 14—Dinner and scientific program at the Memorial Hospital, Worcester, Mass.

April 11—Open date.

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester, Mass.

BOOK REVIEWS

A New Approach to Dietetic Therapy. By EUGENE FOLDES, M.D., Boston. Published by The Gorham Press. 380 pages.

In the preface the author states clearly that this book is the result of inspiration received from a Viennese physicist. Dr. Foldes says that in this book he has utilized theory and fact,—"I believe in the utilizing of theories, provided they be not regarded as facts." The book is divided into three parts. First is a general physio-pathological presentation of water and mineral metabolism in the body; diets; gastro-intestinal tract; internal secretory chain; circulation; respiration; and acid base equilibrium. The second part deals with special pathology; retention and immobilization of water and minerals. For example various disease syndromes; epilepsy, eclampsia, pregnancy, migraine, angina pectoris, gout, essential hypertension and blood disturbances are portrayed. An interesting chapter is entitled "Aging." Part three deals with therapy based on anti-retentional theory and fact. The principle of the anti-retentional plan is practically a presentation of Dr. Joslin's diabetic régime, that is, a person without diabetes ingesting 1 gram of protein per kilogram, ingesting 200 grams of carbohydrate, and low amounts of calories per day, with restricted fluid intake, limited to not more than six glasses of liquid, is carrying out Dr. Foldes' plan. The actual reason or rationale for this dietary suggestion is the reason for the book. In other words, a moderately high protein intake, a moderately low carbohydrate intake, and a very low fat intake with a moderate amount of liquids are supposed to lessen the congestion of cells, which may produce symptoms and signs of disorder. The book is a new approach to the treatment and understanding of certain systemic disturbances. It may be read with great interest by the average physician who is interested in the philosophy of medical problems.

Arteriosclerosis. Published by Joseph Macy, Jr., Foundation. Edited by Edmund V. Cowdry. The Macmillan Company, New York. 1933. 595 pages. Price $5.00.

This book presents contributions made by different men to study the changes in blood vessels generally termed arteriosclerosis. The contributors to this symposium represent all the different phases of scientific and clinical standing. The title is misleading, because if one buys this book with the belief that it is going to be a treatise on arteriosclerosis from a clinical point of view or from a practical, usable point of view, he will be sadly disappointed. It is a compend of arteriosclerosis in which all the various phases ranging from histology to anthropology are reviewed. Many interesting observations, studies, experiments and measurements are presented, but the summary at the back of the book, compiled by Dr. Alfred Cohn of New York, is an excellent piece of work from the point of view of concentrated brevity. However, even he demonstrates the impossibility of taking inconclusive studies and presenting them in a conclusive summary. In one sentence he really reviews the book: ". . . is arteriosclerosis native and natural to man and any attempt at interference or remedy is vain." In other words, it is an intelligent presentation of many facts and theories concerning arteriosclerosis. It is not a practical manual to be bought by any practitioner who expects the alpha and omega of arteriosclerosis including treatment and results to be found between its covers.